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**Thyroid Disorder in Systemic Lupus Erythematosus Patients in  
Southeast Iran.**

Zakeri Z\*, Sandooghi M\*.

\* Assistant Professor, Department of Internal Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.

Correspondence: Dr. M. Sandooghi, Department of Internal Medicine, Zahedan University of Medical Sciences, Zahedan, Iran, Telephone: +98(915) 161-3472, Fax: +98(541) 2442- 185, E-mail: mah-nazsandooghi@yahoo.com

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**Abstract:**

**Background:** We conducted this study to clarify the prevalence of thyroid dysfunction in patients with Systemic Lupus Erythematosus (SLE) and compared it to a matched healthy controls group.

**Material and methods:** Eighty-three SLE and 166 matched healthy controls underwent clinical examination and laboratory evaluation for serum T3, T4, TSH and Thyroid peroxides antibody (TPO AB).

**Results:** 24.1% of SLE patients and 13.3% of control group had thyroid dysfunction (p value = 0.04). Clinical thyroid dysfunction was seen neither in SLE patients nor in the control group. Elevated TSH levels were the most common dysfunction (19.3%) of the SLE, compared with control group (5.4%). Positive TPO antibody was detected in 16.9% of SLE and 16.3% of the control group. Mean level of TPO antibody was higher in SLE patients with thyroid dysfunction (137.05) than SLE patients without the disorder (30.8) (p value=0.007).

**Conclusion:** We concluded thyroid dysfunction was more frequent in SLE patients than in healthy controls. Moreover, SLE patients with anti TPO were more likely to have thyroid dysfunction than the control group.

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**Keywords:** SLE, thyroid dysfunction, hypothyroidism, hyperthyroidism, anti TPO antibody.

## Introduction:

Many SLE patients are initially treated for thyroid dysfunction before the diagnosis of lupus is made or vice versa. Symptoms of thyroid disease can be confused with those of lupus. To identify the thyroid function in lupus patients many studies have been conducted. Although the relationship between autoimmune thyroid disease and SLE has been revealed, the prevalence of thyroid disease in lupus patients is controversial. Reported prevalence of autoimmune thyroid disease (3.9-24%) and anti thyroid antibodies (11-51%) in SLE patients varied considerably.<sup>(1)</sup> A study by Weetmen et al has shown that 51% of SLE patients had thyroid antibodies compared to 27% of controls, and elevated TSH were detected in 25% of SLE patients and 12.5% in the control group.<sup>(2)</sup> In China, prevalence of thyroid antibodies and thyroid dysfunction in SLE patients was 46.7% and 22.2% respectively.<sup>(3)</sup> The prevalence of antimicrosomal and antithyroglobulin antibodies was 32.2% in SLE patients in Singapore.<sup>(4)</sup> In Korean patients with SLE, prevalence of Hashimoto's 'thyroiditis, euthyroid sick syndrome, and graves' disease were 9.5% ,14.3% and 4.8% respectively, while antithyroid antibodies were 27%.<sup>(5)</sup> The study by Chan et al has shown that 13% of SLE patients had subclinical hypothyroidism and 4.3% had hypothyroidism and positive anti TPO were detected in 23.2% of SLE patients.<sup>(6)</sup> In Egypt, ElSharif et al revealed that thyroid disorders in SLE patients were 50% and TPO antibody was found in 15% of SLE patients.<sup>(7)</sup> The aim of this study was to assess the prevalence of thyroid dysfunction and thyroid

antibody in lupus patients in the south-east of Iran compared with a control group. Moreover, in this study we excluded other autoimmune diseases in both SLE patients and the healthy control group to better clarify the association between SLE and thyroid disease.

## Method and Materials:

A case control study was conducted. Eighty-three patients with lupus (without other autoimmune diseases) were selected according to ACR criteria in rheumatologic clinic of Ali- ebn-Abitaleb hospital in Zahedan, Iran. The history for thyroid disorder and drug history for thyroid disease were asked and then participants underwent clinical examination for determination of thyroid size (WHO scoring) and laboratory evaluation for serum T3, T4, TSH and anti TPO antibody. The control group consisted of 166 subjects without SLE being matched in sex and age and were selected from a similar population. Individuals who did not cooperate and those who had other autoimmune diseases (diabetes, rheumatic disease, vitiligo, autoimmune hepatitis) or a history of any thyroid disease were excluded from the study. The included subjects were checked for clinical findings, thyroid hormones and anti TPO antibody. Finally, demographic data and type of thyroid dysfunction was recorded. However, disease activity score, duration of disease, medical therapy, T3RU and free thyroxin level were not detected in SLE patients. The study was approved by the ethical Committee of our institution, and all study participants signed a written informed consent.

### Statistical Analysis:

A t-test was used to compare means of variables. The Chi-Square test and Fisher exact test were also used to compare the frequency of the variables for the two groups. The Mann-Whitney-test was used when necessary. Elevated TSH and suppressed TSH levels were defined by TSH level  $\geq 5$  and TSH  $\leq 0.1$  mic IU / ml, respectively.

### Results:

In the eighty-three SLE patients, mean age was  $30.21 \pm 10.83$  ages (2-63y), seventy-five of whom were female (90.5%) and eight were male (9.5%). In the control group the mean age was  $30.21 \pm 10.83$ , 150 were female (91.0%) and 16 were male (9%). 24.1 % of SLE patients and 13.3% of the control group had thyroid dysfunction (p value = 0.04). Clinical thyroid dysfunction was seen neither in SLE patients nor in the control group. Elevated TSH levels were the most common dysfunction in SLE patients (19.3%) and suppressed TSH was the next most common dysfunction in 4.8% of patients. The prevalence of subclinical hyperthyroidism was 7.8% and subclinical hypothyroidism was 5.4% in the control group. Elevated TSH levels were more common in SLE patients (19.3) compared to the control group (5.4%) (P value = 0.002). Positive TPO antibody was detected in 16.9% of SLE and 16.3% of the control group. Positive anti TPO in SLE patients and the control group with abnormal function was 35% and 22.7% respectively. In other words, a higher frequency of thyroid dysfunction was seen in SLE patients with thyroid

antibody (50.0%) compared with the control group with thyroid antibody (18.5%). Mean level of TPO antibody was higher in SLE patients with thyroid dysfunctions (137.05 IU/mL) than SLE patients without the disorders (30.18 IU/mL) (p value = 0.007). Mean level of TPO antibody in the control group with and without thyroid dysfunctions was 41 IU/mL and 43 IU/mL respectively, which were not statistically significant (p value = 0.95). The distribution of sex and age was similar in both groups. In SLE patients, the size of thyroid was normal in patients with suppressed TSH but it was Grad 1(WHO scoring) in 31.3% of patients with elevated TSH levels and 1.6% of patients with normal TSH. In the control group, abnormal size of thyroid (grad 1 WHO scoring) was seen only in subjects with elevated TSH levels (11.1% of control group).

### Discussion:

In our study 24.1% of SLE patients and 13.3% of the control group had thyroid dysfunction and anti TPO antibody was similar in both SLE patients (16.9%) and in the control group (16.3%). To clarify the association of thyroid disorder and SLE, we excluded other autoimmune disease in both SLE patients and the control group. Unfortunately in this study, serology of free T4 (FTI) and T3RU were not performed, thus the differentiation of subclinical hypothyroidism and euthyroid sick syndrome was not possible. Moreover, this study was short in duration and had a relatively small sample size. In previous studies, reported prevalence of autoimmune thyroid disease (3.9-24%) and anti-thyroid antibodies (11-51%) in

SLE patients varied considerably.<sup>(1)</sup> Early reports were mainly based on short term studies of small cohorts.<sup>(2-6)</sup> However, in our study which was similar to those short term and small cohorts, the prevalence of thyroid dysfunction was in the upper limits of reported prevalence. Two studies have reviewed SLE patients for longer periods of time. In the first study by Miller et al. the prevalence of diagnosed hypothyroidism (6.6%) was unexpectedly high and 18% had high antimicrosomal antibody.<sup>(7)</sup> In the second study by Pyne et al, the prevalence of hypothyroidism in SLE patients (5.7%) was higher than the normal population (1%) while that of hyperthyroidism (1.7%) was not significantly different. Also, 14% had thyroid antibody, rising to 68% in the subgroup who also had thyroid disease.<sup>(1)</sup> In our study the prevalence of thyroid antibody was comparable with these two studies, but we could not find clinical thyroid disease both in patients with SLE and those in the control group. Moreover, our findings contrasted to the study by Chane et al. in which 4.3% of SLE patients had clinical hypothyroidism.<sup>(6)</sup> Also, hypothyroidism was detected in 11.6% of SLE patients compared to 1.9% in the control group in study by Mader et al. However, a statistically significant difference was not observed in the levels of thyroid antibody between the SLE patients and the control group<sup>(8)</sup>, which was compatible with our study. In a recent study by Biro et al. that determined the association of Hashimoto's thyroiditis (HT) and Grave's disease (GD) with systemic autoimmune disease, prevalence of HT in SLE was 90 fold higher than in the gen-

eral population.<sup>(9)</sup> Maybe the reason for low prevalence of clinical hypothyroidism in the population of our study was the exclusion of patients with clinical autoimmune diseases from the control group. Furthermore, there were no coexisting autoimmune diseases in the group of SLE patients. Also, thyroid disease may be less common in southeast Iran, but larger controlled common longitudinal studies are necessary to confirm this. If other autoimmune diseases were not excluded from the group of SLE patients, we would likely find more frequent abnormal thyroid function tests and more severe symptomatic thyroid disease.

In our study, higher frequency of thyroid dysfunction was seen in SLE patients with positive thyroid antibody. Moreover, the level of TPO antibody was higher in SLE patients with thyroid disorder than SLE patients without thyroid disorder which was compatible with some other studies.<sup>(10-12)</sup> This was not seen in the control group. We concluded that thyroid abnormalities were more associated with autoimmune diseases like hypothyroidism (subclinical and overt) or euthyroid sick syndrome in SLE patients. In addition, this finding suggests that detection of high level TPO antibody in SLE patients may help in early detection of associated thyroid disorder. This finding is compatible with a study by Kausman et al. that reviewed the thyroid serology of 150 new cases of SLE patients who were followed up for 7.9 years. On average, 21% were thyroid autoantibody positive. Out of all antibody positive patients, 60% remained persistently thyroid antibody positive. All five cases of clinical thyroid disease, and two out of three cases of subclinical hy-

pothyroidism, occurred in the group with persistently positive thyroid serology.<sup>(12)</sup> In some studies, older age and longer duration of SLE were related to thyroid disorder.<sup>(2, 5, 11)</sup> In our study, mean age was similar in all groups.

### Conclusion:

We concluded that thyroid disorder was more frequent in SLE patients than the healthy control group, although, we excluded other autoimmune diseases. Moreover, SLE patients with anti TPO were more likely to have thyroid dysfunction than the control group. For clarifying the relationship between SLE and thyroid dysfunction, we strongly recommend the following: the study of thyroid dysfunction in the onset of the disease in new cases of SLE patients without other autoimmune diseases; taking history for thyroid disorder and medication for thyroid; and regular follow-up for long periods of time. We also suggest further studies to evaluate prevalence of thyroid disorder in southeast Iran.

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