

**THYROID DYSFUNCTION AMONG PATIENTS WITH SYSTEMIC LUPUS
ERYTHEMATOSUS IN BANGLADESH**Faysal Ahmmed^{1*} and Shahana Ferdous²¹Assistant Professor of Rheumatology, Khulna City Medical College and Hospital, Khulna, Bangladesh.²Assistant Professor of Pediatric Gastroenterology, Khulna City Medical College and Hospital, Khulna, Bangladesh.***Corresponding Author: Dr. Faysal Ahmmed**

Assistant Professor of Rheumatology, Khulna City Medical College and Hospital, Khulna, Bangladesh

Article Received on 08/04/2023

Article Revised on 28/04/2023

Article Accepted on 18/05/2023

ABSTRACT

Background: It's fairly uncommon for one autoimmune illness to coexist with another. Systemic Lupus Erythematosus (SLE) and underactive thyroid are two of the most frequent autoimmune disorders. They could have some kind of connection. **Objective:** To evaluate the association between Thyroid Dysfunction Among Patients with Systemic Lupus Erythematosus in Bangladesh. **Method:** This was a retrospective study in which we reviewed a total 150 patients older than 18 years of age who had a con-firmed diagnosis of SLE according to the Systemic Lupus International Collaborating Clinics classification criteria^[7] and were treated at our rheumatology clinics. Data on clinical manifestations and laboratory findings at the time of presentation were obtained from the medical records of the outpatient clinics of Khulna City Medical College and hospital between January 2022 and December 2022. Data obtained from patients' files included demographic data, sex, age at diagnosis of SLE, history of thyroid dis-eases and treatment for thyroid disease. Laboratory evaluations included complete blood count, thyroid function test (TFT), anti-nuclear antibody (ANA) detection by indirect immunofluorescence, anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody detection with a standardized enzyme-linked immunosorbent assay, serum complement (C3 and C4), TPO and Tg. The Safety of Estrogens in Lupus National Assess-ment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) was used to determine disease activity in patients with SLE. **Results:** During the study, 21-25 years age group, 31%. Followed by 26% belong to >18-20 years age group, 18% belong to 26-30 years age group. Plus majority were female. The main clinical manifestations in our cohort consisted of skin rash in 82 (53.33%), photosensitivity in 55 (36.67%), mucosal ulcers in 36 (34%) and hair loss 30 (20%) patients. 31 patients (20.67%) had thyroid dysfunction. 12 patients (8%) had subclinical hypothyroidism, and 9 patients (6%) had hypothyroidism. Five patients (3.3%) had subclinical hyperthyroidism, and 2 patient (1.33%) had hyperthyroidism. 3 patients (2%) had sick euthyroid status. Besides that, five of nine (55%) patients with hypothyroidism had positive Tg and TPO. One patient with hyperthyroidism tested negative for thyroid auto-antibodies. No association was observed between thyroid dysfunction and SLE disease activity, specifically the SELENA-SLEDAI score, anti-dsDNA level, C3 level and 24-h urine protein. **Conclusion:** We found no association between SLE activity and thyroid problems, but a high prevalence of both subclinical and overt hypothyroid-ism in SLE patients. While treating individuals with SLE, doctors should keep the likelihood of a thyroid problem in mind.

KEYWORDS: Thyroid Dysfunction, Systemic Lupus Erythematosus (SLE), hypothyroidism.**INTRODUCTION**

By a large extent, autoimmune illnesses are the most common medical condition worldwide. Multiple sclerosis, myasthenia gravis, psoriasis, pemphigus vulgaris, lichen planus, alopecia areata, vitiligo, psoriatic arthritis, rheumatoid arthritis, lupus, ankylosing spondylitis, vasculitides, Hashimoto's thyroiditis, graves disease, type 1 diabetes, Addison's disease, ps Possible origins include heredity, epigenetics, the environment, or idiopathic factors (no known cause). They prefer to group together within families due to common origins. Finally, many autoimmune diseases often occur

simultaneously in the same individual. Clinical features of related autoimmune illnesses sometimes overlap and are similar to those of one another. Recognizing the existence of co-morbidities, such as autoimmune diseases, is essential for providing comprehensive and effective therapy. There is evidence connecting hypothyroidism to systemic lupus erythematosus (SLE), two autoimmune diseases.^[4,5] Systemic lupus erythematosus (SLE) is an autoimmune chronic inflammatory disease that may affect any organ or system in the body.^[1,2] Thyroid dysfunction, primarily autoimmune disorders, have been frequently described in

patients with rheumatologic autoimmune diseases, such as SLE, Sjögren's syndrome or rheumatoid arthritis. The prevalence of thyroid dysfunction in SLE varies between 3.8 and 22.2% among different populations and ethnicities. The most common reported thyroid dysfunction in patients with SLE is clinically overt and subclinical hypothyroidism. Several studies evaluating the correlation between thyroid dysfunction and SLE have shown varying and conflicting results.^[3-5] Some studies evaluating the prevalence of anti-thyroglobulin antibodies (Tg) and anti-thyroid peroxidase antibodies (TPO) have shown high thyroid dysfunction in patients with SLE.^[6,7]

Objective

To evaluate the association between Thyroid Dysfunction Among Patients with Systemic Lupus Erythematosus in Bangladesh.

METHODOLOGY

This was a retrospective study in which we reviewed a total 150 patients older than 18 years of age who had a con-firmed diagnosis of SLE according to the Systemic Lupus International Collaborating Clinics classification criteria^[7] and were treated at our rheumatology clinics. Data on clinical manifestations and laboratory findings at the time of presentation were obtained from the medical records of the outpatient at Khulna City Medical College and Hospital, between January 2022 and december 2022.

Data obtained from patients' files included demographic data, sex, age at diagnosis of SLE, history of thyroid diseases and treatment for thyroid disease. Laboratory evaluations included complete blood count, thyroid function test (TFT), anti-nuclear antibody (ANA) detection by indirect immunofluorescence, anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody detection with a standardized enzyme-linked immunosorbent assay, serum complement (C3 and C4), TPO and Tg. The Safety of Estrogens in Lupus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) was used to determine disease activity in patients with SLE. Thyroid dysfunction was clas-sified into three categories according to TFT: sick euthy-roid, hyperthyroidism and hypothyroidism. Hyperthyroidism status was defined by low TSH levels and high values of free thyroxine (T4), free triiodothyronine (T3) or both; or by treatment with carbimazole or propylthiouracil. Hypo-thyroidism was defined by an elevated TSH concentration and low T4 and/or low T3; or by treatment with thyroxine replacement therapy. Thyroid autoantibodies, TPO and Tg were also assessed in patients with abnormal TFT.

RESULTS

Table-1 shows demographic distribution of the patients where 21-25 years age group, 31%. Followed by 26% belong to >18-20 years age group, 18% belong to 26-30 years age group.

Table 1: Demographic distribution of the patients.

Demographic group	Percentage (%)
>18-20 years	26%
21-25 years	31%
26-30 years	18%
31-35 years	16%
>36 years	9%

Figure-1 shows gender distribution of the patients where majority were female 95%.

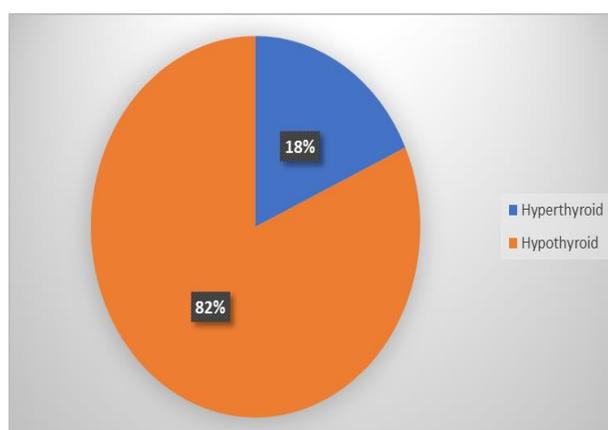


Figure 1: Gender distribution of the patients.

Table-2 shows clinical manifestation of the patients. The main clinical manifestations in our cohort consisted of skin rash in 82 (53.33%), photosensitivity in 55

(36.67%), mucosal ulcers in 36 (34%) and hair loss 30 (20%) patients.

Table 2: Clinical manifestation of the patients.

Clinical manifestation	N	Percentage (%)
Skin rash	82	53.33
Photosensitivity	55	36.67
Mucosal ulcers	36	24
Hair loss	30	20

*multiple responses were noted

Figure-2 shows thyroid dysfunction in patients with SLE where 31 patients (20.67%) had thyroid dysfunction. 12 patients (8%) had subclinical hypothyroidism, and 9 patients (6%) had hypothyroidism. Five patients (3.33%) had hyperthyroidism. Five patients (3.33%)

had subclinical hyperthyroidism, and 2 patient (1.33%) had hyperthyroidism. 3 patients (2%) had sick euthyroid status.

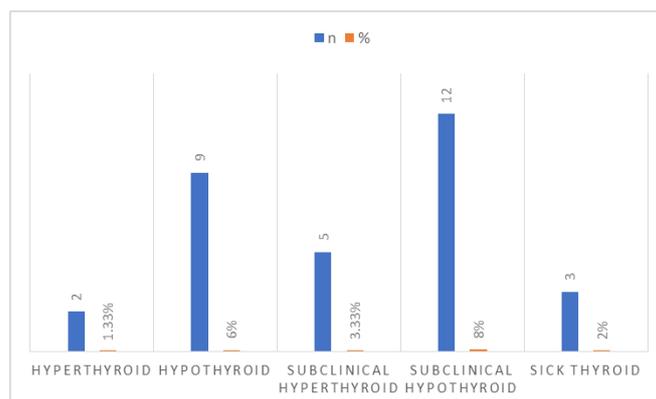
**Figure 2: Thyroid dysfunction in patients with SLE.**

Table-3 shows Thyroid status and thyroid antibodies (Tg and TPO) where five of nine (55%) patients with hypothyroidism had positive Tg and TPO. One patient

with hyperthyroidism tested negative for thyroid auto-antibodies.

Table 3: Thyroid status and the prevalence of thyroid auto-antibodies.

Tg			Negative	Positive
Thyroid Status	Hyperthyroidism	Count	1	0
	Hypothyroidism	Count	5	4
TPO				
Thyroid Status	Hyperthyroidism	Count	1	
	Hypothyroidism	Count	5	4

Table-4 shows Association between thyroid dysfunction and SLE disease activity where No association was observed between thyroid dysfunction and SLE disease

activity, specifically the SELENA-SLEDAI score, anti-dsDNA level, C3 level and 24-h urine protein.

Table 4: Association between thyroid dysfunction and SLE disease activity.

Thyroid status	N	Mean ± SD	P value
Anti-dsDNA:			
Thyroid dysfunction:	25	203.50 ± 491.90	0.775
Normal thyroid function:	125	171.75 ± 306.69	
C3 (0.9–1.8):			
Thyroid dysfunction:	26	0.75 ± 0.39	0.729
Normal thyroid function:	124	0.72 ± 0.59	
24-h urine for protein:			
Thyroid dysfunction:	20	1.94 ± 3.77	0.366
Normal thyroid function:	130	1.15 ± 2.05	
SELENA score:			0.206

Thyroid dysfunction:			
Normal thyroid	25	15.72 ± 10.06	
function:	125	12.79 ± 8.48	

DISCUSSION

SLE patients often struggle with thyroid problems. Thyroid problems are more common in SLE patients than in the general population and have been linked to SLE activity in many studies.^[3,8-11] There is mounting evidence linking SLE to a hereditary predisposition for thyroid diseases. Patients with the R620W polymorphism in the PTPN22 gene encoding a T-cell protein are more likely to have both thyroid illness and SLE.^[12] It has also been shown that individuals with SLE and patients with autoimmune thyroid illnesses have a susceptibility gene at a location on chromosome 5 (5q14.3-15).^[13] Patients with SLE in Bangladesh lack data on the frequency of thyroid dysfunction. Thyroid dysfunction was seen in this research among 31 individuals, or 20.67 percent. Subclinical hypothyroidism was seen in 12 individuals (8%), while hypothyroidism was present in 9 patients (6%). Subclinical hyperthyroidism was seen in 5 individuals (3.5%), while overt hyperthyroidism was present in 2 patients (1.33%). The euthyroid ill percentage was 2%, with 3 cases. Our results are consistent with those of earlier studies.^[1-3, 5, 9, 13-18] which found a rate of hypothyroidism in SLE patients of 3.9-17.4% and a rate of hyperthyroidism in SLE patients of 0.5-8%. Differences in sample size, ethnic groupings, and research design are likely to blame for the substantial heterogeneity seen between studies.

The most common thyroid disorder in our study was subclinical hypothyroidism, which is consistent with the results of a recent meta-analysis comparing 10,500 patients with SLE to 44,170 controls, which found that patients with SLE are more likely to have subclinical hypothyroidism than controls (OR = 5.67, 95% CI = 3.50-9.18).^[8] Nevertheless, some studies have shown that between 15 and 19% of lupus patients had primary hypothyroidism.^[9,14,18] This disagreement might have resulted from different research designs^[9,16] or from using different populations.^[14] Autoimmunity is responsible for almost 80% of the etiology of primary hypothyroidism in lupus patients, as shown by the presence of anti-thyroid antibodies.^[18] In addition, SLE antibodies such anti-dsDNA, anti-RNP, and anti-Smith (Sm) antibody are correlated with ATA levels.^[21] More than two-thirds of Antonelli et al SLE patients who also had hypothyroidism tested positive for anti-thyroid antibodies. Patients with SLE are also more likely to have hypothyroidism than those without the disease.^[14] Pan et al.^[20] found that patients with SLE had greater levels of Tg and TPO than controls. Participants with SLE from the American and European populations were shown to have a higher prevalence of Tg positivity compared to those from the Asian and African populations by further subgroup analysis. TPO positivity has been linked to systemic lupus erythematosus (SLE) in African and European populations but not in

Asian or American populations^[20], indicating that environmental and genetic factors play a different role in each region. In terms of the SELENA-SLEDAI (P = 0.20), anti-ds-DNA (P = 0.77), C3 levels (P = 0.72), and 24-hour urine for protein > 500 mg/day (P = 0.36), our results did not demonstrate a significant link between thyroid disease and SLE disease activity. Our results are in line with a recent research by Mader et al.^[2] who also did not link the SLEDAI to ATA positive. Those with SLE and hypothyroidism fared worse than those with euthyroid and subclinical hyperthyroidism on the Systemic Lupus Activity Measure (SLAM) and SLE Disease Activity Index (SLEDAI)^[21] according to a study of 167 SLE patients. This result contradicts the results of our research, which may be due to selection bias in the study populations. Hashimoto's thyroiditis has been linked to disease activity in a separate study of 63 people with SLE.^[22] In addition, Liu et al. have shown that SLE patients with thyroid problems have an elevated risk of renal and central nervous system involvement.^[3]

CONCLUSION

We found no association between SLE activity and thyroid problems, but a high prevalence of both subclinical and overt hypothyroidism in SLE patients. While treating individuals with SLE, doctors should keep the likelihood of a thyroid problem in mind.

REFERENCE

1. Kumar K, Kole AK, Karmakar PS, Ghosh A. The spectrum of thyroid disorders in systemic lupus erythematosus. *Rheumatol Int*, 2012; 32(1): 73–8.
2. Mader R, Mishail S, Adawi M, Lavi I, Luboshitzky R. Thyroid dysfunction in patients with systemic lupus erythematosus (SLE): relation to disease activity. *Clin Rheumatol*, 2007; 26(11): 1891–4.
3. Liu YC, Lin WY, Tsai MC, Fu LS. Systemic lupus erythematosus and thyroid disease—experience in a single medical center in Taiwan. *J Microbiol Immunol Infect*, 2019; 52(3): 480–6.
4. Rasaei N, Shams M, Kamali-Sarvestani E, Nazarinia MA. The prevalence of thyroid dysfunction in patients with systemic lupus erythematosus. *Iran Red Crescent Med J*, 2015. <https://doi.org/10.5812/ircmj.17298>.
5. Boey ML, Fong PH, Lee JSC, Ng WY, Thai AC. Autoimmune thyroid disorders in SLE in Singapore. *Lupus*, 1993; 2(1): 51–4.
6. Pyne D, Isenberg DA. Autoimmune thyroid disease in systemic lupus erythematosus. *Ann Rheum Dis*, 2002; 61(1): 70–2.
7. Weetman AP, Walport MJ. The association of autoimmune thyroiditis with systemic lupus erythematosus. *Br J Rheumatol*, 1987; 26(5): 359–61.

8. Luo W, Mao P, Zhang L, Yang Z. Association between systemic lupus erythematosus and thyroid dysfunction: a meta-analysis. *Lupus*, 2018; 27(13): 2120–8.
9. Watad A, Cohen AD, Comaneshter D, Tekes-Manova D, Amital H. Hyperthyroidism association with SLE, lessons from real-life data—a case-control study. *Autoimmunity*, 2016; 49(1): 17–20.
10. Franco JS, Amaya-Amaya J, Molano-González N, et al. Autoimmune thyroid disease in Colombian patients with systemic lupus erythematosus. *Clin Endocrinol (Oxf)*, 2015; 83(6): 943–50.
11. Posselt RT, Coelho VN, Skare TL. Hashimoto thyroiditis, anti-thyroid antibodies and systemic lupus erythematosus. *Int J Rheum Dis*, 2018; 21(1): 186–93.
12. Domingues SL, Gonçalves FT, Jorge MLMP, Limongi JE, Ranza R, Jorge PT. High prevalence of hypothyroidism in systemic lupus erythematosus patients without an increase in circulating anti-thyroid antibodies. *Endocr Pract*, 2017; 23(11): 1304–10.
13. Watad A, Mahroum N, Whitby A, et al. Hypothyroidism among SLE patients: case-control study. *Autoimmun Rev*, 2016; 15(5): 484–6.
14. Antonelli A, Fallahi P, Mosca M, et al. Prevalence of thyroid dysfunction in systemic lupus erythematosus. *Metabolism*, 2010; 59(6): 896–900.
15. Chan AT, Al-Saffar Z, Bucknall RC. Thyroid disease in systemic lupus erythematosus and rheumatoid arthritis. *Rheumatology (Oxford)*, 2001; 40(3): 353–4.
16. Tsai RT, Chang TC, Wang CR, Chuang CY, Chen CY. Thyroid disorders in Chinese patients with systemic lupus erythematosus. *Rheumatol Int*, 1993; 13(1): 9–13.
17. Lin WY, Chang CL, Fu LS, Lin CH, Lin HK. Systemic lupus erythematosus and thyroid disease: a 10-year study. *J Microbiol Immunol Infect*, 2015; 48(6): 676–83.
18. Klionsky Y, Antonelli M. Thyroid disease in lupus: an updated review. *ACR Open Rheumatol*, 2020; 2(2): 74–8.
19. Konstadoulakis MM, Kroubouzos G, Tosca A, et al. Thyroid autoantibodies in the subsets of lupus erythematosus: correlation with other autoantibodies and thyroid function. *Thyroidology*, 1993; 5(1): 1–7.
20. Pan XF, Gu JQ, Shan ZY. Patients with systemic lupus erythematosus have higher prevalence of thyroid autoantibodies: a systematic review and meta-analysis. *PLoS One*, 2015; 10(4): e0123291.
21. Liu H, Yang LH, Yin G, Xie QB. Correlation of thyroid autoantibodies, systemic lupus erythematosus immunologic indicators and disease activity in SLE with HT. *Sichuan Da Xue Xue Bao Yi Xue Ban*, 2018; 49(2): 179–82.
22. Pillai S, Velayudhan G. Thyroid dysfunction in SLE and association of thyroid antibody levels with disease activity in sSLE. *J Evolut Med Dental Sci*, 2017; 6: 2684–8.