

ORIGINAL RESEARCH

Prevalence of thyroid dysfunction in patients with systemic lupus erythematosus

Manohar Joshi¹, Akanksha Saberwal²

¹Associate Professor, Department of General Medicine, DY Patil University School of Medicine, Nerul, Navi Mumbai, India.

²Associate Professor, Department of ENT, DY Patil University School of Medicine, Nerul Navi Mumbai, India.

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, the pathogenesis of which remains elusive. Recently, many studies have indicated that the prevalence of thyroid dysfunction is higher in SLE patients than in the general population. Present study was aimed to study prevalence of thyroid dysfunction in patients with systemic lupus erythematosus. **Material and Methods:** Present study was descriptive, cross-sectional observational study, conducted in patients attending OPD / IPD, diagnosed cases of SLE by Systemic Lupus International Collaborating Clinics 2012 lupus classification criteria. **Results:** In present study, 63 SLE patients were studied. Among 63 patients, only 3 were male (4.76 %), rest were female (95.24 %) & mean age was 34.56 ± 11.95 years. Prevalence of autoantibodies was noted as ANA (77.78 %), dsDNA (57.14 %), %, Anti-TPO (34.92 %) & Anti-Tg (30.16 %), In present study, normal TSH levels was 0.35-5.5 μ IU/ml, normal fT3 levels was 2.1-4.4 pg/ml & normal fT4 levels was 0.7-1.8 ng/dl. In present study, abnormal TSH levels noted in 16 cases (high – 22.22 % & low- 3.17 %), abnormal fT3 levels noted in 14 cases (low – 20.63 % & high- 1.59 %) & abnormal fT4 levels noted in 18 cases (high – 1.59 % & low- 26.98 %). Thyroid dysfunction was noted in 27 cases (42.86 %), majority had subclinical hypothyroidism (17.46 %), clinical hypothyroidism (11.11 %) & subclinical hyperthyroidism (1.59 %), while anti- TPO alone elevated noted in 8 cases (12.7 %). **Conclusion:** There is a greater possibility of missing the diagnosis of thyroid dysfunctions in SLE patients, as both the diseases have similar clinical manifestations. We noted higher incidence of thyroid dysfunctions in SLE patients.

Keywords: thyroid dysfunctions, SLE patients, autoimmune, hypothyroidism

Corresponding Author: Dr. Manohar Joshi, Associate Professor, Department of General Medicine, DY Patil University School of Medicine, Nerul, Navi Mumbai, India.

Email: drjoshimanohar@gmail.com

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, the pathogenesis of which remains elusive. Manifestations of SLE can involve the skin, joints, kidney, central nervous system, cardiovascular system, serosal membranes and hematologic and immune systems. The disease is highly heterogeneous, with patients manifesting variable combinations of clinical features.¹

Due to the advancement in diagnosis and treatment, the mortality rate of SLE has been greatly reduced. However, the mortality rate in SLE patients was still three times higher than that in the general population.² Multisystem organ involvement and tissue damage in SLE is mediated by the deregulation of self-reactive B-cells, resulting in autoantibody production, immune complex disposition, and complement activation.³

The deficiency or excess of thyroid hormone is defined as thyroid dysfunction, including (subclinical) hypothyroidism and (subclinical) hyperthyroidism. Autoimmune factors are likely to be relevant to the development of SLE and thyroid dysfunction. Recently, many studies have indicated that the prevalence of thyroid dysfunction is higher in SLE patients than in the general population.^{4,5,6} Present study was aimed to study prevalence of thyroid dysfunction in patients with systemic lupus erythematosus.

MATERIAL AND METHODS

Present study was descriptive, cross-sectional observational study, conducted in patients attending Rheumatology clinic under Department of Medicine, at DY Patil University School of Medicine, Nerul, Navi Mumbai, India. Study duration was of 4 years (January 2019 to December 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients attending OPD / IPD, diagnosed cases of SLE by Systemic Lupus International Collaborating Clinics 2012 lupus classification criteria⁷, willing to participate in present study

Exclusion criteria

- Patients receiving medications that are known to cause thyroid dysfunction,
- Patients with history of thyroidectomy,
- Patients receiving SLE with pregnancy
- Patients with systemic autoimmune diseases

Study was explained to patients in local language & written consent was taken for participation & study. Detailed clinical history, medical history, comorbidities and clinical examination findings were noted in case record proforma. The following investigations were performed. CBC, LFT, RFT, urine (specific gravity and broad cast), Peripheral smear for anaemia and burr cells, Serum calcium and phosphorus, Serum cholesterol, serum protein, ECG and chest X ray, USG abdomen were done in all patients. 5 ml of blood sample is collected in non-heparinised serum bottle and sent for thyroid profile. Serum triiodothyronine, serum thyroxine, serum thyroid stimulating hormone. The levels of TSH, total triiodothyronine (T3), total thyroxine (T4), antinuclear antibody (ANA), antibodies to double stranded DNA (dsDNA), anti- thyroglobulin antibodies (anti- Tg) and anti-thyroid peroxidase (anti-TPO) were measured by Enzyme linked immunosorbent Assay & chemiluminescent microparticle immunoassay. All assays were carried out in central clinical biochemistry.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS

In present study, 63 SLE patients were studied. Among 63 patients, only 3 were male (4.76 %), rest were female (95.24 %) & mean age was 34.56 ± 11.95 years. Prevalence of autoantibodies was noted as ANA (77.78 %), dsDNA (57.14 %), Anti-TPO (34.92 %) & Anti-Tg (30.16 %),

Table 1: General characteristics

Variables	No. of patients	Percentage
Mean Age (years)	34.56 ± 11.95	
Gender		
Male	3	4.76
Female	60	95.24
Autoantibodies		
ANA	49	77.78
dsDNA	36	57.14
Anti-TPO	22	34.92
Anti-Tg	19	30.16
Autoantibody titre		
ANA (IU/mL)	2839.5 ± 1754.3	
Anti dsDNA (IU/mL)	16345.5 ± 10892.1	
Anti-TPO (IU/mL)	129.42 ± 34.55	
Anti-Tg (IU/mL)	282.82 ± 170.25	

In present study, normal TSH levels was 0.35-5.5 µIU/ml, normal fT3 levels was 2.1-4.4 pg/ml & normal fT4 levels was 0.7-1.8 ng/dl. In present study, abnormal TSH levels noted in 16 cases (high – 22.22 % & low- 3.17 %), abnormal fT3 levels noted in 14 cases (low – 20.63 % & high- 1.59 %) & abnormal fT4 levels noted in 18 cases (high – 1.59 % & low- 26.98 %).

Table 2: Thyroid function test reports

Variables	No. of patients	Percentage
TSH		
Normal	47	74.6
High	14	22.22
Low	2	3.17
fT3		
Normal	49	77.78
High	13	20.63
Low 1	1	1.59
fT4		
Normal	45	71.43
High	17	26.98
Low 1	1	1.59

Thyroid dysfunction was noted in 27 cases (42.86 %), majority had subclinical hypothyroidism (17.46 %), clinical hypothyroidism (11.11 %) & subclinical hyperthyroidism (1.59 %), while anti- TPO alone elevated noted in 8 cases (12.7 %).

Table 3: Thyroid dysfunction

Groups	FT4	TSH	n	Percentage
Clinical hypothyroidism	Reduced	Elevated	7	11.11
Subclinical hypothyroidism	Normal	Elevated	11	17.46
Hyperthyroidism	Elevated	Reduced	0	0
Subclinical hyperthyroidism	Normal	Reduced	1	1.59
Anti- TPO alone elevated	normal	normal	8	12.7

DISCUSSION

SLE is a multisystemic disease and can involve any organ in the body including the thyroid gland.^{7,8} The pathogenesis of SLE is considered to be influenced by many factors, such as genetic, hormonal and environmental factors. Because autoimmunity plays an important role in the pathogenesis of SLE, an association between this disorder and thyroid autoimmunity may exist.⁹

Autoimmune diseases can be divided into organ-specific and systemic illness. The systemic inflammatory autoimmune diseases are RA, SLE, dermatomyositis, polymyositis and systemic sclerosis. One of the most common organs to be affected by organ-specific autoimmune injury is the thyroid gland.¹⁰ Because of its autoimmune nature, other autoantibodies such as anti-TPO and anti-Tg can be produced during the natural course of disease.^{4,5} Autoimmune thyroid disease (AITD) frequently coexists with other systemic autoimmune conditions such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Several studies demonstrated that patients with SLE have increased prevalence of thyroid dysfunction and autoimmune thyroiditis.⁴⁻⁹ While some studies reported a higher prevalence of hyperthyroidism in SLE patients,¹¹ others reported a higher prevalence of hypothyroidism.^{1,4,5,6,12} Most of the studies present in the literature show a high prevalence, and incidence, of new cases of hypothyroidism and autoimmune thyroiditis (AT) in systemic lupus erythematosus (SLE) patients, overall in female gender.¹³

Desai AS et al.,¹⁴ studied 100 SLE patients, 99 were females, and most (47%) belonged to the age group of 20–30 years, the median duration of lupus was 24 months. Thyroid dysfunction was observed in 42% (n = 42), and hypothyroidism was the most common thyroid abnormality. Among the patients with thyroid dysfunction, the corresponding number of patients with clinical hypothyroidism and subclinical hypothyroidism were 71% (n = 30) and 29% (n = 12). Of 25 patients with elevated anti-TPO, 48% (n = 12) had clinical hypothyroidism, 20% (n = 5) had subclinical hypothyroidism, and 32% (n = 8) had normal thyroid-stimulating hormone and free T4. Most of the patients with thyroid dysfunction were newly diagnosed, and the predominant symptoms noted were fatigue (75%), hair loss (75%), and joint pain (63%).

Jamil Ul H¹⁵ studied 50 patients, 49 were females, and most (47%) belonged to the age group of 20–30 years, the median duration of lupus was 24 months. Thyroid dysfunction was observed in 42% (n = 21), and hypothyroidism was the most common thyroid abnormality. Among the patients with thyroid dysfunction, the corresponding number of patients with clinical hypothyroidism and subclinical hypothyroidism were 71% (n = 15) and 29% (n = 6). Of 13 patients with elevated anti-TPO, 46% (n = 6) had clinical hypothyroidism, 23% (n = 3) had subclinical hypothyroidism, and 30% (n = 4) had normal thyroid-stimulating hormone and free T4.

Nakisa R et al.,¹⁶ conducted a case-control study. The mean age of SLE patients and controls were 32.16 ± 9.19 and 32.48 ± 9.47 years, respectively ($P = 0.821$). Patients had significantly higher prevalence (43.2% vs. 23.9%; $P = 0.015$) and titers (221.8 ± 570.5 vs. 78.2 ± 277.2 ; $P = 0.036$) of antibodies to Tg compared to controls. The patients had significantly lower titers of T3 compared to controls (125.2 ± 35.6 vs. 136.2 ± 26.5 ; $P = 0.021$). The titers of T4, TSH and anti-TPO antibody did not differ significantly between the two study groups. Thyroid dysfunction was not higher in SLE patients compared to healthy individuals. However, anti-Tg antibodies were higher in SLE patients.

In a meta-analysis¹⁷ of 1076 systemic lupus erythematosus cases and 1661 healthy controls, showed that the prevalence of thyroid autoantibody positivity in patients with systemic lupus erythematosus was higher than in healthy controls (TgAb: OR = 2.99, 95% CI = 1.83–4.89; TPOAb: OR = 2.20, 95% CI = 1.27–3.82, respectively). In other meta-analysis¹⁸ Ten studies with 10,500 SLE patients and 44,170 healthy controls were included in this study. The meta-analysis results showed that the prevalence of (subclinical) hypothyroidism in SLE patients was higher than in the healthy controls (hypothyroidism: OR = 2.93, 95% CI = 1.81–4.75; subclinical hypothyroidism: OR = 5.67, 95% CI = 3.50–9.18). No statistical difference of (subclinical) hyperthyroidism was found between SLE patients and controls.

In SLE patients with thyroid disease, Isenberg et al showed that the serological status of a significant minority of patients fluctuates and patients may become thyroid antibody negative with time.¹⁹ This subgroup is unlikely to develop clinical thyroid disease Many patients of autoimmune thyroid disease have anti-nuclear antibodies (ANA) in their sera (78%)²⁰, a fact to be remembered while investigating vague complaints like fatigue, hair loss and arthralgias, all of which may be due to hypothyroidism and ANA positivity too may be due to autoimmune thyroid disease and not SLE.

Notably, our study has several limitations such as observational, single-center study, small sample size, lack of some information regarding demographic data among patients who were diagnosed with thyroid dysfunction & lack of a control group. Further studies concentrating on improving clinical and biochemical criteria to diagnose thyroid dysfunction in SLE patients are needed.

CONCLUSION

There is a greater possibility of missing the diagnosis of thyroid dysfunctions in SLE patients, as both the diseases have similar clinical manifestations. We noted higher incidence of thyroid dysfunctions in SLE patients. Simultaneous occurrence of thyroid disorder with SLE bears diagnostic and therapeutic significance.

REFERENCES

1. 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 Nov;26(11):1891-4.
2. Yurkovich M, Vostretsova K, Chen W, Aviña-Zubieta JA. Overall and Cause-Specific Mortality in Patients With Systemic Lupus Erythematosus: A Meta- Analysis of Observational Studies. *Arthritis Care Res (Hoboken)* (2014) 66 (4):608–16.
3. Pillai SS, Velayudhan G. Thyroid dysfunction in SLE and association of thyroid antibody levels with disease activity in SLE. *J Evolution Med Dent Sci* 2017;33;2684-8.
4. Pyne D, Isenberg DA. Autoimmune thyroid disease in systemic lupus erythematosus. *Ann Rheum Dis*. 2002;61(1):70–2.
5. Antonelli A, Fallahi P, Mosca M, Ferrari SM, Ruffilli I, Corti A, et al. Prevalence of thyroid dysfunctions in systemic lupus erythematosus. *Metabolism*. 2010;59(6):896–900.
6. Appenzeller S, Pallone AT, Natalin RA, Costallat LT. Prevalence of thyroid dysfunction in systemic lupus erythematosus. *J Clin Rheumatol*. 2009;15(3):117–9.
7. Ighe A, Dahlström Ö, Skogh T, Sjöwall C. Application of the 2012 systemic lupus international collaborating clinics classification criteria to patients in a regional swedish systemic lupus erythematosus register. *Arthritis Res Ther* 2015;17:3.
8. Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med*. 2003;349(16):1526–33.

9. Al-Motwee S, Jawdat D, Jehani GS, Anazi H, Shubaili A, Sutton P, et al. Association of HLA-DRB1*15 and HLADQB1*06 with SLE in Saudis. *Ann Saudi Med.* 2013; 33: 229–234.
10. Paul R, Raychaudhuri P, Sinha PK, Mookerjee S, Pandit K, Santra G. Prevalence of systemic lupus erythematosus among patients of hypothyroidism in a tertiary care center. *Indian J Endocr Metab* 2012;16:569-74.
11. Chan AT, Al-Saffar Z, Bucknall RC. Thyroid disease in systemic lupus erythematosus and rheumatoid arthritis. *Rheumatology (Oxford).* 2001;40(3):353–4.
12. Al-Awadhi AM, Olusi S, Hasan EA, Abdullah A. Frequency of abnormal thyroid function tests in Kuwaiti Arabs with autoimmune diseases. *Med Princ Pract.* 2008;17(1):61–5.
13. Ferrari SM, Elia G, Virili C, Centanni M, Antonelli A and Fallahi P (2017) Systemic Lupus Erythematosus and Thyroid Autoimmunity. *Front. Endocrinol.* 8:138.
14. Desai AS, Chandy S, Pakalomattom SJ, Shobha V. Prevalence of thyroid dysfunction in patients with systemic lupus erythematosus: A descriptive cross sectional study. *Indian J Rheumatol* 2020;15:79-83.
15. Jamil Ul Hussain (2022) 'Prevalence of Thyroid Dysfunction In Patients With Systemic Lupus Erythematosus', *International Journal of Current Medical and Pharmaceutical Research*, 08(02), pp 62-65.
16. Nakisa Rasaei, Mesbah Shams, Eskandar Kamali-Sarvestani, Mohammad Ali Nazarinia, The Prevalence of Thyroid Dysfunction in Patients With Systemic Lupus Erythematosus, *Iran Red Crescent Med J.* 2015 December; 17(12): e17298.
17. Pan X-F, Gu J-Q, Shan Z-Y (2015) Patients with Systemic Lupus Erythematosus Have Higher Prevalence of Thyroid Autoantibodies: A Systematic Review and Meta-Analysis. *PLoS ONE* 10(4): e0123291.
18. Luo W, Mao P, Zhang L, Yang Z. Association between systemic lupus erythematosus and thyroid dysfunction: a meta-analysis. *Lupus.* 2018;27(13):2120-2128.
19. Pyne D, Isenberg DA. Autoimmune thyroid disease in systemic lupus erythematosus. *Ann Rheum Dis* 2002; 61:70
20. Rudrajit Paul, Pradip Raychaudhuri, Pradip Kumar Sinha, Sekhar Mookerjee, Kaushik Pandit, Gouranga Santra. Prevalence of systemic lupus erythematosus among patients of hypothyroidism in a tertiary care center. *Indian J Endocrinology and Metabolism* 2012; 16:569-574.