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Thyroid Dysfunction In Systemic Lupus Erythematosus And Its Relation To Severity

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is the prototypic systemic autoimmune disease with multisystem involvement. Autoimmune thyroiditis is characterized by a slowly progressive asymptomatic phase followed by complete destruction of the thyroid gland manifesting as overt hypothyroidism. Thyroid disorders in SLE may escape early detection and treatment due to similar clinical features, hampering the symptomatic relief.

Methods: This is a hospital based observational study in the department of Medicine over a period of one year in 76 SLE Patients with test for TSH, FT4 and FT3 and thyroid autoantibodies- Anti TPO and complements level. Severity of SLE was assessed with SLEDAI Score.

Results: Thyroid dysfunction was noted in 31.6% subjects in our study(n=24).
The commonest dysfunction was primary hypothyroidism in 14.5%, followed by subclinical hypothyroidism in 9.2% study subjects. Anti TPO antibodies in serum were present in 35.5% of SLE patients of which thyroid dysfunction was found in 48.1% subjects. Significant correlation was observed between thyroid dysfunction and severity of SLE. (P Value <0.05)

Conclusion: The prevalence of thyroid dysfunction in SLE
patients is higher compared to normal population, it is mostly autoimmune in nature and associated significantly with severity of SLE as assessed by SLEDAI score.

Keywords: Autoimmune Thyroiditis, SLE, Thyroid dysfunction

Introduction

The association of SLE with other autoimmune diseases is likely due to the underlying pathophysiology of autoimmunity. McDonagh in his study cited that 30% of patients of SLE had at least one other autoimmune disease[1]. Vianna J cited the coexistence of high titer of antithyroid antibodies in patients of SLE[2] The presence of anti-DNA antibodies and antinuclear antibodies in patients with Graves' disease and Hashimoto's thyroiditis with no clinical signs of SLE have also been reported.[3]

Prevalence of SLE range in between 20 to 240 per 100,000 people (Firestein and Kelley's Textbook of Rheumatology)

Various studies have shown higher prevalence of thyroid dysfunction in patients with SLE than in the general population[4–6] . Thyroid disease can affect the course of disease progression in SLE. Dong et al in his study showed that a delay in initiation of treatment of subclinical hypothyroidism can delay remission of disease in SLE.[7] In the present study, we intend to estimate the prevalence and pattern of

thyroid dysfunction in SLE along with its effect on the severity of SLE in patients attending a tertiary care center in North East India.

Materials And Methods:

Study Design - Observational Study

Study Setting - Department of Internal Medicine, Gauhati Medical College, Guwahati, Assam, India.

Study period – June 2021 to May 2022

Study Group:

The study sample comprised of 76 newly diagnosed or follow up patients of systemic lupus erythematosus who had attended medicine O.P.D./Ward or Rheumatology O.P.D. and

fulfilled the inclusion and exclusion criteria. Informed consent of the participants of the study was taken in written format.

Inclusion Criteria:

1. Diagnosed cases of SLE as per SLICC criteria

2. Patients >12 years of age.

Exclusion Criteria:

1. Patients with past history of thyroid surgery or radiotherapy.

2. Patients taking drugs which alter thyroid function tests.

3. Pregnancy

4. Patients not willing to participate in the study.

Method Of Study:

The diagnosis of Systemic lupus erythematosus was made according to the SLICC (SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINIC) Criteria.

The patients in the study group were assessed with thyroid function tests by FT4 (free thyroxine), FT3

(free tri iodothyronine), TSH (thyroid stimulating hormone) and thyroid autoantibodies (anti-TPO). The thyroid hormones were estimated by chemiluminescent immunoassay (CLIA).

Disease activity was assessed by using SLEDAI Index-SYSTEMIC LUPUS

Erythematosus Disease Activity Index.

Autoimmune thyroid disorder (AITD) was confirmed by the presence of circulating

Anti-TPO in the serum of patients with thyroid disorder.

Thyroid abnormalities were categorised as :

1. Elevated TSH with low FT4 - Primary hypothyroid
2. Elevated TSH with normal FT3/FT4 - Subclinical hypothyroid
3. Low TSH with raised FT3/FT4 - Primary hyperthyroid
4. Low TSH with normal FT3/FT4 - Subclinical hyperthyroid.

Other pattern of thyroid function abnormality not fitting with the above pattern was categorised under sick euthyroid group (classically with low T3,normal TSH and T4).

Data Analysis:

Data analysis was done using SPSS (IBM Corporation Version 23).

Results:

Age and Gender wise distribution of the study population:

Of the 76 patients, 89.5 % were females and 10.5% were males. The mean age of the study population was 26.3 years (± 6.6yrs).

Prevalence and Pattern of Thyroid dysfunction:

Thyroid dysfunction was present in 31.6% of patients in the study (24 nos).

The pattern of thyroid dysfunction observed was as follows: (TABLE 1)

Primary hypothyroidism – 14.5% (11 subjects)

Subclinical hypothyroidism – 9.2% (7 subjects)

Primary hyperthyroidism - 2.6% (2 subjects)

Subclinical hyperthyroidism- 1.3%(1 subject)

Sick euthyroid - 3.9% (3 subjects)

Prevalence of autoimmunity in relation to thyroid dysfunction:

Of the total 76 patients, thyroid autoimmunity defined as presence of Anti TPO Antibodies in serum were present in 27 study subjects (35.5%).

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Of the 24 patients with thyroid dysfunction, only 13 (54.2%) were positive for antibodies and hence autoimmune in nature.(Autoimmune thyroid disease)

14 patients (26.9 %) had presence of anti TPO antibody in the serum, but no thyroid dysfunction.

Thyroid dysfunction relation to duration of SLE:

Mean duration of SLE in the study subjects was 2±1.2 years. The mean disease duration of SLE in those with thyroid dysfunction was 2.8 years and in those without thyroid dysfunction was 1.4 years.

Relation between thyroid dysfunction and severity of SLE:

The mean SLEDAI score in thyroid dysfunction group was 11.3 and in euthyroid group was 4.5 with p value of 0.001.

Thyroid status in relation to complements level in SLE:

Out of total 76 patients, 30.2% (23 nos) patients had low complements level,

17.3% (43 nos) of SLE patients without any thyroid dysfunction had low complements level while 58.3% (14 nos) patients with thyroid dysfunction had low complements level.

Table 1: Prevalence And Pattern Of Thyroid Dysfunction:

Interpretation	Frequency	Percent
Euthyroid	52.0	68.4%
Primary Hypothyroidism	11.0	14.5%
Primary Hyperthyroidism	2.0	2.6%
Sick euthyroid	3.0	3.9%
Subclinical hypothyroidism	7.0	9.2%
Subclinical hyperthyroidism	1.0	1.3%
Total	76.0	100.0%

Table 2: Prevalence And Pattern Of Thyroid Disease In SLE In Various Studies

STUDY	NO OF CASES	PRIMARY HYPO THYROIDISM (%)	SUBCLINICAL HYPO THYROIDISM (%)	PRIMARY HYPER THYROIDISM (%)	SUBCLINICAL HYPER THYROIDISM (%)
Miller et Al[15]	332	6.6	39	3	-
Kumar Et al[6]	100	14	12	-	2
Park Et al[16]	63	9.5	1.6	4.8	-
Appenzeller	524	5.3	11.5	-	-

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et al[17]					
Porkodi Et Al[18]	153	7.8	2.6	1.3	-
Our Study	76	14.5	9.2	2.6	1.3

Table 3: Prevalence Of Autoimmune Thyroid Disease In Different Studies:

STUDY	NO OF CASES	THYROID DYSFUNCTION (%)	AUTOIMMUNE THYROID DISEASE (%)
Weetman Et al[19]	41	-	24.3
Park et al[20]	61	-	14.3
Kumar Et al[6]	100	36	30

Discussion:

76 patients of SLE were studied for the presence of thyroid dysfunction, thyroid antibodies in serum and disease severity in this study. Patients were grouped into euthyroid (no thyroid dysfunction), primary/overt hypothyroid, subclinical hypothyroid, primary/overt hyperthyroid, subclinical hyperthyroid and sick euthyroid. Patients with sick euthyroid were considered under thyroid dysfunction group in this study based on thyroid function test report, but these patients were not treated for thyroid disorder during the critically ill period.

Of the 76 patients, 68 (89.5%) were females and 8 (10.5%) were males. In our study, female to male ratio was 8.5:1. **Malviya et al 1988** reported a female to male ratio of 8:1 in their study, and **Weckerle and Niewold et al 2012** reported a female: male ratio of 9:1 in their study.[8]

Status of thyroid dysfunction :

Thyroid dysfunction was noted in 31.6% subjects in our study(n=24). The prevalence of hypothyroidism in Indian population has been reported to be 11%.[9] The prevalence of hypothyroidism in lupus patients in our study has been found to be higher as compared to the normal population in all age groups as per data available.

Mader et al 2007 reported a prevalence of 11.6% for hypothyroidism in SLE patients, a finding higher than the prevalence in normal population.[10] **Kumar et al 2010** found thyroid dysfunction in 36% of lupus patients with primary hypothyroidism being the commonest dysfunction (14%).[6] (TABLE 2)

Presence of thyroid autoimmunity and Autoimmune thyroid disease:

Thyroid autoimmunity characterised by presence of anti TPO antibodies in serum were present in 35.5% of SLE patients (27 nos) in our study out of which thyroid dysfunction was found in 48.1% subjects(13 nos).

This is comparable to findings of **30.4% and 30%** (prevalence of anti TPO antibodies) in studies done by **Hoogendoorn et al 2006** and **Kumar et al 2010**.[6,11]

Of the 24 subjects with thyroid dysfunction in our study, 54.1% (13 subjects) had autoimmune thyroid

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disease. Rest 45.9% (11 subjects) were non autoimmune in nature.

Of the 11 patients with primary hypothyroidism, 63.6% (7nos) had autoimmune thyroid disease and 71.4% (5 nos) in subclinical hypothyroid group had autoimmune thyroid disease. Subclinical hyperthyroidism and sick euthyroid were not associated with autoimmunity. Similar studies mentioning the prevalence of autoimmune thyroid disease are mentioned in Table 3.

Duration of disease in relation to thyroid dysfunction:

Mean duration of disease was 2±1.2 years. Mean disease duration of SLE in euthyroid patients was 1.4years while in those with thyroid dysfunction was 2.8years.

Domingues et al and Goncalves et al 2017 has observed a higher duration of SLE in patients with thyroid dysfunction, a finding comparable to our study.[12]

Disease severity and thyroid dysfunction in SLE:

As per SLEDAI score, a score of 1-5 was considered as mild disease, a score of 6-10 was considered moderate disease activity while score of 11-19 was considered as high disease activity and score of >/20 as very high disease activity.

The mean SLEDAI score in subjects in our study was 7.04 ±4.6.

Our study found a significant mean difference between SLEDAI score in thyroid dysfunction (11.3) and euthyroid group (4.5) with p value of 0.001 suggesting a significant association between disease severity and thyroid dysfunction.

Magaro et al 1992[13] found higher prevalence of hypothyroidism and antiTPO antibody in patients with active disease.

Thyroid dysfunction and complements level:

17.3% (43 nos) of SLE patients without any thyroid dysfunction had low complements level while 58.3% (14 nos) patients with thyroid dysfunction had low complements level.

Thyroid dysfunction was associated with hypocomplementemia, with p value of 0.001 suggesting significant negative correlation of thyroid dysfunction with complements level.

Liu and Yang et al 2018 found a negative correlation between C4 and thyroid autoantibody and a positive correlation between C3 and FT3[14]

Conclusion:

It was concluded from our study that the prevalence of thyroid dysfunction in SLE patients is higher as compared to normal population and it is mostly autoimmune in nature. Thyroid dysfunction in SLE is also significantly associated with severity of SLE as assessed by SLEDAI score and complements level. As SLE and thyroid dysfunction share many common clinical features, thyroid dysfunction in SLE may escape early detection. Routine thyroid function testing in SLE may help in early detection of thyroid disorders, thereby facilitating early treatment and better symptom relief of the patients. Also, early detection may help in predicting the severity of SLE.

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