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RESEARCH ARTICLE

A cross-sectional study to know the prevalence of thyroid dysfunction in systemic lupus erythematosus

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a persistent autoimmune disease, the pathogenesis of which remains elusive. Autoimmune factors may be a cause of SLE and thyroid dysfunction. Many studies have revealed that the prevalence of thyroid disorder is higher in SLE patients than in the general population. SLE is a multisystem and hypothyroidism is an organ specific autoimmune disorder and can occur successively or simultaneously. **Aims and Objectives:** The aim of the study was to study the prevalence of thyroid disorder in patients with SLE. **Materials and Methods:** Patients admitted with definite clinical features of SLE and Antinuclear Antibodies positive, in medicine ward and healthy blood donors are taken as control. Sample was tested by fully automated analyzer. **Results:** Subclinical hypothyroidism was found in 24% of study group and 8% of control group which is statistically significant. Central and secondary hyperthyroidism was found in 10% of study group and 12% of control group but it was statistically insignificant. Several studies have documented an association between SLE and other autoimmune diseases such as Sjogren's syndrome, autoimmune hemolytic anemia, and antiphospholipid syndrome. Subclinical hypothyroidism was higher than another thyroid dysfunction such as primary, central, and subclinical hypothyroidism was found to be higher in frequency, probably depicting the slow destructive process which is pathognomic of autoimmune thyroiditis. **Conclusion:** Subclinical hypothyroidism was more prevalent in SLE than that of overt hypothyroidism as compared with general population.

KEY WORDS: Systemic Lupus Erythematosus; Hypothyroidism; Autoimmunity

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder. The etiogenesis of which is unknown. Subclinical hypo and hyper thyroidism are defined as deficiency or excess of thyroid hormones, respectively, in blood. Autoimmunity is related to the pathogenesis of SLE and thyroid dysfunction.[1] Many studies showed that thyroid dysfunction is higher in SLE than in general population. Objective of our study is to reveal the prevalence of thyroid disorder in SLE.

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Clinical features of SLE are quite variable, mild form seen in joint and skin, and severe form found in internal organ damage. Persistent inflammation leads to irreversible damage and ultimately increases the morbidity and mortality. This disease can be reduced by proper therapeutic strategies. These goals can be achieved by better understanding of disease pathogenesis and follow-up.

Hypothyroidism is organ-specific and SLE is a multisystem autoimmune disorder.[2,3] They can occur consecutively or simultaneously. Majority of studies found that thyroid disorder was more common in patients with SLE than in the general population.

SLE with hypothyroidism as the initial clinical presentation is uncommon. In the literature review, it was found that the prevalence of clinical hypothyroidism in SLE ranges from 3 to 21.4%. This study suggested for clinical diagnosis, attention should be given to screening for hypothyroidism in SLE. Thyroid dysfunction should be considered as an important factor in the treatment of SLE.

Due to modulation of the lymphocytic activity by estrogen it mainly affects the women of child bearing age group, and the female: Male ratio of 10–15:1 was found.[4]

Environmental and genetic factor promotes immune system activation and damages the different organ which leads to the increased incidence of morbidity and mortality. Over the years, it has been seen that SLE patients have increased incidence of thyroid dysfunction than the general population.[5,6]

Autoimmune thyroiditis (AT) produces antibodies such as anti-Ro antibodies antinuclear antibodies (ANA), anti-double-stranded DNA anti-cardiolipin antibodies and others. AT produces goiter due to infiltration with lymphocytes, inflammatory changes in thyrocytes, and fibrosis.[7] AT leads to hypothyroidism and is associated with elevated TSH levels and thyroid enlargement. Thyroid stimulating immunoglobulins cause Graves' disease.

Fifty ANA-positive patients with simultaneous thyroid studies were revealed (88% female, 93% Caucasian, mean age 11.9 ± 4.0 years). Half of patients had an ANA titer ≥1:320. 30% of patients had thyroid antibodies. About 29% anti-thyroglobulin (ATG) and 21% anti-thyroid peroxidase (ATPO) was detected in the patients; among these 14% were children with hypothyroidism. Anti-thyroid antibodies were not associated with positivity of ANA pattern and titer.[8-11]

Chronic lymphocytic thyroiditis among ANA-positive children has ATG and ATPO, significantly higher (30%) without a rheumatologic condition compared to the general pediatric population (1.3–3.4%). Presence or absence of thyroid antibodies is unrelated to ANA titer and pattern did not help to predict anything. Thyroid antibodies and increased incidence of developing hypothyroidism over time, routine estimation of ATG and ATPO, and thyroid function tests among ANA-positive children are necessary.[12,13] Auto-antibodies that target substances inside cells are called ANA. The test detects auto-antibodies directed against components of the nucleus and also other cellular components that are contained within the cell cytoplasm, outside nucleus.[14-17]

Autoimmune disorders manifestation often vary among patients and so difficult to diagnose. Careful history taking and examination of a patient's, physical findings, and other test results, a positive ANA screening may help in the diagnosis of autoimmune diseases.[18]

Auto immune thyroid dysfunction and SLE have been carried out in several research works with difference of opinion. Some studies reported an elevated prevalence of hyperthyroidism in SLE, others reported hypothyroidism. Higher prevalence of hypothyroidism with SLE is not associated, compared with general population. Anti-thyroid antibodies (ATA), such as ATG antibodies and anti-thyroid peroxidase antibodies (TPO), was associated with higher incidence in SLE. Results were analyzed in the light of the prevalence of these findings in the general population and not with SLE-affected person.

Objectives

The aim of the study was to find out the prevalence of thyroid dysfunction in SLE person.

MATERIALS AND METHODS

This was a cross-sectional, observational, and single-centered study to analyses the prevalence of thyroid disorders among SLE patients. Patients admitted with definite clinical features of SLE and ANA positive, in medicine ward as per selection criteria of the study population, each patient who meets the inclusion criteria and does not fall in the exclusion criteria will be selected. Moreover, healthy blood donors are taken as control.

Inclusion Criteria

Patients diagnosed as Systematic lupus erythematosus according to SLICC criteria were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patients unwilling to participate
2. Patient with active infection
3. Patient with other autoimmune disease
4. Hematological disorder.

RESULTS

Out of 100 randomly selected subjects, 50 (50.0%) were SLE patients and rest 50 (50.0%) of the subjects were from the healthy subjects without any clinical manifestations of diseases.

Student's "*t*" test showed that there was no significant difference in mean age of the participants of the two groups

(t = 1.62; P = 0.11). Thus, the participants of the two groups were matched for their ages. Chi-square test showed that there was no significant association between level of FT4 in the participants of the two groups (P = 0.10). Thus, level of FT4 was more or less equally distributed over the participants of the two groups. There was no significant difference in mean level of FT4 of the participants of the two groups (t = 1.29; P = 0.20) as revealed by the "t" test Table 1.

Chi-square test showed that there was statistically significant association between level of TSH and the participants of the two groups (P = 0.0075). Thus, high level of TSH among the cases (40.0%) was significantly higher than normal (16.0%) (Z = 3.77; P < 0.001). "t"-test showed the mean level of TSH of the cases was statistically higher than the controls (t 2.64; P = 0.0107) Table 2. About 70.0% of the patients were with age between 20 and 39 years which was statistically higher than other age groups. Thus, in this study, SLE was mostly prevalent in the age group 20–39 years. The male: female was 1:49. Test of proportion showed that females (98.0%) were statistically higher than males (2.0%) (Z = 13.57; P < 0.0001). Thus, the finding of this study suggests that females were at higher risk for SLE.

Most of the patients were with euthyroid (42.0%) followed by sub-clinical hypothyroidism (24.0%) which were significantly higher than other status of thyroid (Z = 2.63; P = 0.0083) Tables 3 and 4. Thus, in this study, the prevalence of thyroid disorder with SLE was 58.0%.

DISCUSSION

The present study aimed to determine if there is any increased association of thyroid abnormalities with SLE. Fifty subjects were included as cases in this study and were assessed by clinical and biochemical parameters. All these subjects were cautiously screened for the presence of thyroid disorder. We also analyzed 50 persons from general population for thyroid dysfunction with in similar age distribution and sex. The prevalence of thyroid disorder and its clinical correlation with SLE was analyzed using Chi-square test. In our study, subclinical hypothyroidism was higher than another thyroid dysfunction such as primary and central hypothyroidism. Subclinical hypothyroidism was found to be more common in frequency, probably depicting the slow destructive pathogenesis which is more pathognomic of AT. Thyroid dysfunction was highest among 30–40 years of age group patients. Overt hypothyroidism was only 10% which could be due to slow evolving process of autoimmunity leads to overt hypothyroidism. The prevalence of subclinical hypothyroidism is 24% in our study which is higher than control group (4%). A study conducted by Tsai *et al*.[6] in Chinese patients found that there is a higher prevalence of hypothyroidism (10.4%) which is similar to our findings. Few recent studies have addressed the query if there is any association between antithyroid antibodies with SLE. The prevalence of Anti TPO Ab in the case group was 16% comparable to 32.2% and 31% in studies conducted by Kabelitz *et al*.,[9] Tsai *et al*.,[6] respectively. Between the activity of the disease with the presence of antithyroid antibodies, an association was also found.[19,20] About 70% of SLE patients showed thyroid autoantibodies.[21,22] Hashimoto's thyroiditis and SLE also have antithyroid autoantibodies.[23] There are very few studies in India regarding the association between thyroid disorder and SLE. Kumar *et al*.[24] found 36% association of thyroid dysfunction compared to 8% of controls which was similar to our study. Primary hypothyroidism was the most common disorder (14%) while subclinical hypothyroidism was more common as depicted in our study. This study is almost parallel except for the more prevalence of subclinical hypothyroidism. Hence, autoimmune thyroid disorder should be screened for organ-specific and organ non-specific autoimmune antibodies. Patients with SLE have more prevalence of subclinical hypothyroidism and positive

Table 1: FT4 level in case and control groups

Level of FT4	Case	Control
Mean±SD	1.23±0.58	1.46±0.37
Median	1.07	1.495
Range	0.56–4.50	0.67–2.78

x^2=4.53; P=0.1 (Statistically not significant)

Table 2: Level of TSH in case and control groups

Level of TSH	Case	Control
Mean±SD	5.50±6.42	3.04±1.48
Median	3.7	3.055
Range	0.80–35.00	0.82–8.00

x^2=7.14; P=0.0075 (Statistically significant)

Table 3: Correlation of thyroid dysfunction with Anti-DS DNA in cases

Thyroid dysfunction	Anti DS DNA levels		Total
	Normal and low	High	
Present, *n* (%)	13 (26)	16 (32)	29 (58)
Absent, *n* (%)	8 (16)	13 (26)	21 (42)
Total, *n* (%)	21 (42)	29 (58)	50 (100)

P=0.7734 (not significant) fisher exact test

Table 4: Diagnostic distribution of the patients as per status of thyroid function

Status of thyroid function	Number	%
Euthyroid	21	42.0
Sub-clinical hypothyroidism	12	24.0
Central hypothyroidism	5	10.0
Primary hypothyroid	5	10.0
Sick euthyroid syndrome	4	8.0
Secondary hyperthyroidism	3	6.0
Total	50	100.0

thyroid auto-antibodies.[19,20] Thyroid auto-antibodies may leads to the appearance of clinical autoimmune disorder. SLE and thyroid disease symptomatically may be similar. Routine investigation of SLE patients is done with the screening for autoimmune thyroid disorder.[21] High-risk women (positive Ab TPOs) should be evaluated by thyroid function, follow-up, and appropriate treatment in due course.[19]

CONCLUSION

SLE was associated with statistically significant thyroid disorder and autoimmune dysfunction when compared with the general population. Subclinical hypothyroidism was more prevalent in SLE than that of overt hypothyroidism as compared with general population. Age, sex, and period of SLE may be significantly related to thyroid autoimmunity.

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