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Research Article

PREVALENCE OF THYROID DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Background: Estimate of prevalence of thyroid dysfunction in systemic lupus erythematosus (SLE) patients from India is scarce. The present study evaluated the prevalence of thyroid dysfunction and anti-thyroid peroxidase (TPO) antibodies in SLE patients, and the most prominent clinical features of thyroid dysfunction were noted.

Materials and Methods: This descriptive, cross-sectional study involved 50 adult patients diagnosed with SLE in government medical college and associated hospital Rajouri Jammu and Kashmir india. The study excluded patients on medications that are known to cause thyroid dysfunctions, those with a history of thyroidectomy, and those with other systemic autoimmune diseases.

Results: Among the 50 recruited 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. None of the patients had hyperthyroidism. 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. 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%).

Conclusions: The prevalence of thyroid dysfunction was found to be higher in SLE than previously published cohorts in India and the rest of the world. It does not affect lupus activity.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder affecting women in their reproductive years.[1]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.[2]

Many studies have demonstrated that autoimmune thyroid diseases marked by the presence of anti-thyroid antibodies are associated with various rheumatological disorders.[3]Goh and Wang in 1986 have reported that thyroid disorders are more prevalent in SLE patients than in general population.[4]In a recent review and was noted among SLE patients compared with the general population (odds ratio of 2.93; $P < 0.05$). This included ten studies with 10,500 SLE patients and 44,170 healthy controls. In addition, 5.67-fold increased the risk of subclinical hypothyroidism based on five studies was documented. The relationship between SLE and hyperthyroidism as well as subclinical hyperthyroidism is inconclusive at present.[5]

Although several studies reported increased prevalence of thyroid disease in SLE patients, it has not been established whether the occurrence of SLE functions as an independent risk factor for developing thyroid abnormalities. In addition, it has not been studied whether the association

Prevalence studies evaluating the prevalence of thyroid dysfunction in Indian SLE patients are very limited. An Indian study by Pillai and Velayudhan, conducted in 100 SLE patients, has reported hypothyroidism (26%) as the common thyroid abnormality noted, followed by subclinical hypothyroidism (24%) and hyperthyroidism (16%).[2]Kumar *et al*. reported that primary hypothyroidism (14%) and subclinical hypothyroidism (12%) were the most common alterations among lupus patients, which was significantly higher when compared to control group (5% and 3%, respectively).[6]The present study was intended to estimate the prevalence of thyroid abnormalities, anti-thyroid peroxidase (TPO) antibodies, and the most prominent clinical features of thyroid dysfunction in SLE patients attending medical college Rajouri J&k india

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MATERRIALS AND METHODS

The descriptive, cross-sectional observational study was conducted at Government medical college and associated hospital Rajouri, Jammu and Kashmir India. The study recruited 50 consecutive adult SLE patients fulfilling Systemic Lupus International Collaborating Clinics 2012 lupus classification criteria.[7]Patients receiving medications that are known to cause thyroid dysfunction, and those with a history of thyroidectomy, SLE with pregnancy and subject with systemic autoimmune diseases were excluded from the study.

Complete clinical assessment, with a specific focus on features of hypothyroidism or hyperthyroidism, was conducted for all the enrolled patients and details entered into a prestructured pro forma. SLE Disease Activity Index-2K (SLEDAI-2K) was calculated for all patients.[8]Specific laboratory investigations included the estimation of free T4 (FT4), thyroid-stimulating hormone (TSH), and anti-TPO antibody. Patients were classified as hyperthyroidism (clinical and subclinical), clinical hypothyroidism, subclinical hypothyroidism, and those with elevated anti-TPO alone using standard definitions.[9]Overt hypothyroidism was defined as TSH levels >10 lU/L and subclinical hypothyroidism as elevated TSH (5–10 lU/L) with normal (FT4 10–28 pmol/l) as per the laboratory cutoffs. Five TSH and FT4 were tested using a chemiluminescence enzyme immunoassay. Anti-TPO antibody levels were tested using chemiluminescent microparticle immunoassay. All assays were carried out in the laboratory of the department of clinical biochemistry and swastik diagnostic laboratory kacchi chawni jammu which is national accredited laboratory

Statistical analysis

Descriptive statistical analysis was conducted to calculate the mean, standard deviation, and percentage, wherever appropriate. The prevalence of different thyroid dysfunctions and anti-TPO status in recruited patients was calculated as proportion or percentage.

Chi-square test was used to for comparing different groups. Probability value <5% was considered as statistically significant. The analysis was performed using SPSS version 18 software (SPSS Inc., USA).

RESULTS

Of the 50 recruited SLE patients, 49 were women; and majority of the patients (47%) belonged to the age group of 20–30 years. Duration of SLE ranged from newly diagnosed to 14 years, the median duration of lupus being 24 months. The duration of hypothyroidism ranged from newly diagnosed to 19 years [Table 1].

Table 1 Distribution of the subjects based on duration of SLE and dysfunction

Disease duration(years)	no. of SLE patients n=50	no patient with thyroid dysfunction n=50
<1	23	15
1-5	19	6
6-10	7	3
>10	1	1

Among the total enrolled patients, 25 patients were found to have thyroid dysfunction. Thyroid dysfunction was detected before the diagnosis of SLE in 12 (48%) of the patients, whereas in 6 (24%), thyroid dysfunction was detected after the SLE diagnosis. Both the diseases were diagnosed simultaneously in 7 (28%) of the patients. The time relation between the onset of SLE and thyroid dysfunction is shown in Figure 1.

Hypothyroidism was the most common thyroid abnormality noted, and none had hyperthyroidism. Among the patients with thyroid dysfunction, the corresponding number of patients with clinical hypothyroidism and subclinical hypothyroidism were 60% (n = 15) and 24% (n = 6) [Table 2]. Overall, elevated anti-TPO levels were noted in 13 patients. Among them, the prevalence of clinical hypothyroidism, subclinical hypothyroidism, and normal TSH and FT4 were 48% (n = 6), 20% (n = 3), and 32% (n = 4), respectively [Table 3].

Table 2 Patient distribution based on different thyroid dysfunctions

Groups	FT4	TSH	*n*	Percentage
Clinical hypothyroidism	Reduced	Elevated	15	60
Subclinical hypothyroidism	Normal	Elevated	06	24
Hyperthyroidism	Elevated	Reduced	0	0
Subclinical hyperthyroidism	Normal	Reduced	0	0
Anti-TPO alone elevated	normal	normal	04	16

Table 3 Distribution of the subjects based on the anti-TPO status

Groups	*n*	Percentage
Anti-TPO normal	75	75
Anti-TPO high with clinical hypothyroidism	12	12
Anti-TPO high with subclinical hypothyroidism	5	5
Anti-TPO alone elevated	8	8

Fatigue (75%), hair loss (75%), and joint pain (63%) were the predominant symptoms reported in patients with thyroid dysfunctions. Among all the symptoms, statistical significance was noted for joint pain (P = 0.02) and constipation (P = 0.02). Overall, of 8 patients with neurological manifestations, 5 fulfilled american college of rheumatology (ACR) neurological criteria for neuropsychiatric systemic lupus erythematosus,[10]which included psychosis (n = 3), peripheral neuropathy,[2]and hemiplegia, seizure, and cerebral venous thrombosis one each. Thyroid dysfunction was documented in two of them. Of one patients with Carpal Tunnel syndrome had overt hypothyroidism. Serositis was noted in 6 patients in overall cohort, three of them had thyroid dysfunction. Pleural effusion and pericardial effusion were reported in three and one patients, respectively, and two patients had both. Largely, classical manifestations of hypothyroidism such as weight gain, constipation, and delayed tendon jerks were conspicuous by their absence.

Table 4 Comparative data Demographic characteristics, Thyroid Dysfunction and prevalence of anti TPO antibody

Variables	Porkodi *et al.*[6] (n=153)	Kumar *et al.*[5] (n=100)	Osama *et al.*[3] (n=80)	Appenzeller *et al.*[4] (n=524)	Adriana *et al.*[11] (n=100)	Miller *et al.*[12] (n=332)	Present study (n=100)
Age in years (Mean±SD)	29.5 (17-35)	26.6 (±9.42)	33.4±11.3	28.8±11	34 (15-73)	35.4 (11-74)	29.4±9.3
Disease duration (Mean)	26 months (SLE) (Thyroid)	55.5 months	40.8 (±45.83) months	NA	6.2 years	6.1 years	5 years 2 years (SLE) 0 years (thyroid)
Female: Male	100:0	88:12	10.4:1	Predominantly females	13.2:1	94:6	99:1
Thyroid dysfunctions (%)	13.1	36	25	6.1	22	7.5	42
Hypothyroidism (%)	7.8	14	8.7	87	4	6.6	30
Subclinical Hypothyroidism (%)	2.6	12	13.7	11.5	10	39	12
Hyperthyroidism (%)	1.3	0	1.25	0	0	3	0
Subclinical Hyperthyroidism (%)	0	2	1.25	0	2	NA	0
Anti-TPO alone elevated (%)	1.3	18	NA	17	6	NA	8

Only one patient had hypothyroidism in family. None had a family history of lupus. None of autoantibodies

(Immunoblot-EUROIMMUN) correlated with thyroid dysfunction or the presence of anti-TPO.

The mean SLEDAI-2K in the entire cohort was 7.2 (±5.6) with a range from 0 to 26. There was no significant difference in SLEDAI scores between euthyroid and thyroid dysfunction group ($P = 0.19$).

DISCUSSION

It is well established that SLE is significantly associated with thyroid dysfunction, specifically hypothyroidism and subclinical hypothyroidism. We explored this association in our cohort of lupus patients.

The mean age of patients enrolled in the present study was 29.4 ± 9.3 years, and most of them belonged to the age group of 20–30 years. In contrast to other studies from India (Kumar *et al*. and Porkodi *et al*.), we report an overall higher prevalence of thyroid dysfunction, overt hypothyroidism (30%) and subclinical hypothyroidism (12%) in our cohort. However, none had hyperthyroidism in our cohort. Elsewhere, Khataybeh *et al*., Kakehasi *et al*., and Miller *et al*. have observed subclinical hypothyroidism as the major thyroid abnormality, but to a much lesser extent [Table 4].[11-13]
In stark contrast to these findings, the 10-year study by Lin *et al*. have reported that the rate of thyroid diseases was significantly lesser in SLE patients (8.1% vs. 16.9%; $P < 0.001$) when compared to non-SLE-matched controls.[14] Several studies have reported inconsistent findings on the association between thyroid autoimmunity and SLE. Most of these individual studies were not powerful enough to determine the association and had relatively small sample size. Recently published systemic meta-analysis aimed at providing reliable estimates of the extent of any association has corroborated the hypothesis, suggesting an increased thyroid autoimmunity risk in SLE patients.[15]

Higher prevalence of thyroid dysfunction noted in the present study could be attributed to higher prevalence of thyroid disorders in Asians than the Western population raising the risk over and above the ethnic predisposition. It could also be attributed to significantly higher female to male ratio of the present study, as hypothyroidism is 4–5 times more common in females than males.[16,17]A study at st, johns medical collegehospital, bengalaru, karnataka conducted on 100 patients of rheumatoid Arthritis, 15% were detected as overt hypothyroidism, 5% subclinical hypothyroidism, while hyperthyroidism was detected in 1%.[18]In a population-based study done in Cochin, India, the prevalence of hypothyroidism was 3.9% and that of subclinical hypothyroidism was 9.4% in 971 iodine-sufficient adults.[17]The prevalence was higher, at 11.4% in women, when compared with men, in whom the prevalence was 6.2%.

In the present study, 48% of the patients were detected with thyroid dysfunctions before the diagnosis of SLE; whereas in 22% of the patients, the dysfunctions were detected after the detection of SLE. In 30% of the patients, both the diseases were diagnosed simultaneously. Porkodi *et al*. have demonstrated that thyroid dysfunction preceded SLE in 30%, postdated in 40%, while the concurrent diagnosis was made in 30%.[14]The study by Antonelli *et al*. has noted the diagnosis of autoimmune disease at SLE onset in 2.9% of patients, and 70.6 % of patient developed thyroid disease during follow – up dysfunction in This might be attributed to high index of suspicion and ease of availability of thyroid assays.

Of the 50 SLE patients, elevated anti-TPO levels were noted in 13 (26%) patients. Among them, 4 (31%) patients had normal thyroid function tests, 6 had clinical hypothyroidism, and 3 had subclinical hypothyroidism. Based on the literature evidence, a review by Blich *et al*. has concluded on the increased prevalence of anti-TPO antibodies in SLE patients than in the general population. Anti-TPO autoantibodies play a crucial role in the diagnosis of autoimmune thyroid diseases and in estimating the disease course. Kohno *et al*. have reported that the anti-TPO autoantibody specificities noted in SLE are different from that in thyroid disorders.[20]

The prominent attributable symptoms of thyroid dysfunctions noted in the present study patients were as follows: fatigue (75%), hair loss (75%), and joint pain (63%). These symptoms are frequent in lupus population too and undetected thyroid dysfunction may contribute to persistent symptoms. Goh and Wang also noted a higher incidence of joint pain, mucocutaneous involvement, lymphadenopathy, and renal manifestations in SLE patients with thyroid dysfunction.[4]

Lack of a control group for comparison was one of the major limitations of the study. The skewed enrollment of female patients in the present study is attributed to increased preponderance of SLE in females than males. The study has not matched the clinical and SLE-related antibody profiles with that of the thyroid antibody profile due to the limited sample size, which would have helped in further corroborating the association.

Corroborating this association and thereby, early detection and treatment for both the diseases would be beneficial for planning therapeutic strategies.

CONCLUSIONS

In summary, the present study underscores the need for conducting thyroid function and TPO antibody tests as part of the biochemical and immunological profiling of SLE patients. Moreover, there is a greater possibility of overlooking the diagnosis of thyroid dysfunctions in SLE patients, as both the diseases have similar clinical manifestations. Further studies involving larger population are warranted to substantiate this association.

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Conflicts of interest

There are no conflicts of interest.

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