

Thyroid Dysfunction and Thyroid Autoantibodies in Egyptian Patients with Systemic Lupus Erythematosus (SLE)

Ayman Abd El-Aziz¹, Mostafa Abd Elal Doma²,

Abdel Hamead A. Mohammed³, and Essam A. El-Moselhy^{4*}

Internal Medicine¹, Rheumatology, Physical Medicine & Rehabilitation², Clinical Pathology and Community Medicine³, Faculty of Medicine, Al-Azhar University

*Corresponding Author: Ayman Abd El-Aziz, Department of Internal Medicine, Al-Azhar University, Egypt.

e-mail: d.aymann.abdelaziz@hotmail.com

ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with many clinical manifestations and immunological abnormalities. SLE and autoimmune thyroid disease are at the two endpoints of a shared immunogenetic mechanism. **Aim of the study:** To evaluate the link between SLE and thyroid disorders. **Patients and Methods:** Thirty patients known to have SLE were recruited in this study, with age ranged from 17 to 35 years. All patients were submitted to history taking, clinical examination, and relevant laboratory investigation. **Results:** Thyroid disorders were common (33.3%) in lupus patients. Hypothyroidism was the commonest (16.6%) abnormality in SLE patients then euthyroid (10.0%), and lastly hyperthyroidism (6.6%). The mean age of SLE patients was 26.1±1.5 year. Eighty percent of the patients were females. The most common SLE characteristics were malar flush (90.0%), photosensitivity (80.0%), fever (70.0%), and arthritis (50.0%). Mean Hb level was 9.2±0.59 g/dL. While, mean values of acute phase reactants were erythrocyte sedimentation rate (ESR) at 1st and 2nd hour (74.3±6.6 and 121.4±5.26 mm/h, respectively) and C-reactive protein (20±6.7 mg/L). The means of FT₃, FT₄, TSH, TG Ab, and anti thyroperoxidase (TPO) Ab in SLE patients were 136.6±14.1 ng/dL, 8.83±1.2 ng/dL, 4.15±1.27 ng/dL, 15.12±11.15 ng/dL, and 121±65.4 IU/mL, respectively. Meanwhile, 30.0% and 76.7% of SLE patients were +ve for rheumatoid factor (RF) and antineuclear Ab, respectively. There were 6.7% and 16.7% of the patients +ve for thyroglobulin Ab and anti TPO Ab, respectively. The statistically significant differences parameters in SLE patients with normal and abnormal thyroid function were ESR at 1 & 2 hours, RF, and anti TPO Ab (P=0.00, 0.00, 0.03, and 0.03, respectively). The statistically significant differences parameters of demographic, clinical, and laboratory data in SLE patients with normal and subgroups of abnormal thyroid function were age, SLE duration, Hb level, RBC, WBC, PLT, and ESR at 1 & 2 hours (P=0.00, 0.00, 0.00, 0.001, 0.0001, 0.00, 0.00, and 0.00, respectively). **Conclusion and Recommendation:** Thyroid disorders are common in SLE patients. The most common form is hypothyroidism. Patients with SLE should be evaluated for thyroid disorders by testing FT₃, FT₄, TSH, TG Ab, and anti TPO Ab for early detection of thyroid abnormalities. Further studies are needed to support and clarify the association between SLE and thyroid disorders.

Key words: Systemic lupus erythematosus, Clinical manifestations, Thyroid dysfunction.

INTRODUCTION

Autoimmune diseases can be divided into organ-specific and systemic illness. The systemic inflammatory autoimmune diseases are such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), etc [1]. SLE is prevalent throughout the world with manifold clinical manifestations and immunological abnormalities. SLE is affecting primarily women [2]. Its incidence varies from 40-100 per 1, 00,000 population [3]. Also, thyroid disorders are quite common. They are the next common to type 2 diabetes mellitus among the various endocrine disorders [4]. Many studies had showed the prevalence of thyroid disorders in SLE [5,6]. SLE Patients had a high prevalence of symptomatic and significantly more subclinical hypothyroidism and positive thyroid autoanti-

bodies. Thyroid autoantibodies may precede the appearance of clinical autoimmune disease [7]. Also, thyroiditis is very common in SLE [8]. Hashimoto's disease (HD) is the most important autoimmune cause of thyroiditis all over the world. The patients often present with hypothyroidism and a firm goiter. It is the most common cause of goitrous hypothyroidism in areas of iodine sufficiency [9]. Thyroiditis and consequent hypothyroidism can be the first manifestation of a variety of autoimmune diseases such as Sjogren's syndrome, Scleroderma and SLE [6]. Pyne and Isenberg [10] showed that patients with SLE had a prevalence of hypothyroidism greater than that of the normal population. The presence of either condition was associated with a higher frequency of both antimicrosomal and anti-thyroglobulin antibodies (anti TG Abs).

Infections were among the main complications of SLE [11].

The mechanism for autoimmune destruction of the thyroid probably involves both cellular immunity and humoral immunity. Lymphocytic infiltration of the thyroid gland by B cells and cytotoxic T cells is a common histologic feature of all forms of autoimmune thyroiditis. Autoimmune thyroiditis is linked to HLA-DR 3,4,5 that are also linked to SLE [8].

Various rheumatologic manifestations such as arthritis, joint swelling, muscle pain, and swelling are common in hypothyroidism particularly in patients with HD. Also, thyroiditis is often associated with other autoimmune diseases such as SLE, RA, etc [12]. Further, thyroid function abnormalities and thyroid autoantibodies have been frequently described in patients with rheumatologic autoimmune diseases, such as RA, SLE, and scleroderma [13].

SLE is often associated with thyroiditis features and hypothyroidism. On the other hand, patients of hypothyroidism with rheumatological symptoms may have other auto-immune disease such as SLE and RA in addition [5]. Result of a metaanalysis suggests that thyroid autoimmunity is more prevalent in patients with SLE than in a control group [14]. Also, subclinical hypothyroidism is significantly higher among SLE patients than in healthy controls [15]. The screening for SLE can perhaps help us in identifying the etiology of hypothyroidism in a substantial proportion of cases, especially in the presence of significant goiter [1].

Aim of the work

The aim of this work is to assess the thyroid function and thyroid autoantibodies in Egyptian patients with SLE in Assiut Governorate.

PATIENTS AND METHODS

A descriptive, analytical study design was used to investigate the present research problem. An approval was taken to conduct the present study from the Councils of the Departments of the Internal Medicine and the Rheumatology, Physical Medicine & Rehabilitation, Al-Azhar University, Assiut, Egypt. Also, the Medical Ethics Committee of Al-Azhar Faculty of Medicine, Assiut, Egypt has approved protocol of the study. The study was conducted on thirty patients with SLE attending the Outpatient Clinics of the Internal Medicine and the Rheumatology, Physical

Medicine & Rehabilitation, Al-Azhar University Hospital at Assiut. The patients were seeking for medical advice or follow up. All patients were known to have SLE. Aim of the study and procedures that will be done were explained to the patients. All patients accepted to participate in the study and an informal consent was taken from each of them. The study was done during period from October 2014 to February 2015.

The patients were subjected to the following:

A. Determine their demographic characteristics.

B. Full history taking; personal, present, past, and family history.

C. Full clinical examination; general, local, and other systems examination.

D. Laboratory investigations:

1- Erythrocyte sedimentation rate (ESR) at 1 & 2 hours and C-reactive protein (CRP) (using latex method for both of them).

2- Complete blood count (CBC) using cell counter.

3- Rheumatoid factor (RF) using ELISA (IU/mL).

4- Thyroid function tests; free T₃ (ng/dL), free T₄ (µg/dL), and TSH (µIU/mL) using Cobas method.

5- Thyroid antibodies tests: Thyroglobulin antibodies (TG Ab, µIU/mL) and anti thyroperoxidase (anti TPOAb IU/mL) using Cobas method.

6- Antinuclear antibodies (ANA, using ELISA, IU/mL).

Exclusion criteria

A- The patients who already has thyrotoxic graves disease.

B- The patients who are under steroid medication.

Statistical analysis

Analysis of data was done by computer using Epi-info, software, version 6.04. The data were presented in 7 tables and one figure. Tabulated data were presented as frequency distribution and percentage, range, and arithmetic mean (M) ± standard deviation (SD). Student's t-test (testing the statistical significance difference between two means ± SD of two samples) and F-test (analysis of variance, ANOVA) testing the statistical significance of difference between three Ms ± SD of three groups) were used. Chi-square (χ²) test or Fisher Exact (FE) test (they testing for the statistical significant relation between different variables' grades in quantitative data or percentages). If

the obtained P-value of the t-test, F-test, χ^2 , and FE were ≤ 0.05 ; so the difference between the groups was considered significant and if it was > 0.05 ; the difference between the groups was considered insignificant.

RESULTS

Table (1) shows the demographic and clinical data of patients with systemic lupus

erythematosus. Age of the patients ranged from 17 to 37 years, with mean 26.1 ± 1.5 . As regard to sex, 24 (80.0%) were females and 6 (20.0%) were males. Mean duration of the disease was 12.8 ± 2.6 month. Lastly, table (1) and figure (1) clear that the most common characteristics of SLE features were malar flush (90.0%), photosensitivity (80.0%), fever (70.0%), and arthritis (50.0%).

Table (1): Demographic and clinical data of patients with systemic lupus erythematosus (SLE)

Variables	SLE patients (N=30)
	N (%) or (M± SD)
Age (years)	
Range	17 – 37
Mean ± SD	26.1 ± 1.5
Sex	
Male	6 (20.0%)
Female	24 (80.0%)
Disease duration time (Mean±SD month)	12.8 ± 2.6
Characteristic (complaint) features of SLE	
Malar flush	27 (90.0%)
Photosensitivity	24 (80.0%)
Arthritis	15 (50.0%)
Discoid lupus	11 (36.7%)
Oral ulceration	9 (30.0%)
Serositis	9 (30%)
Fever	21 (70.0%)
Renal disorders	14 (46.7%)

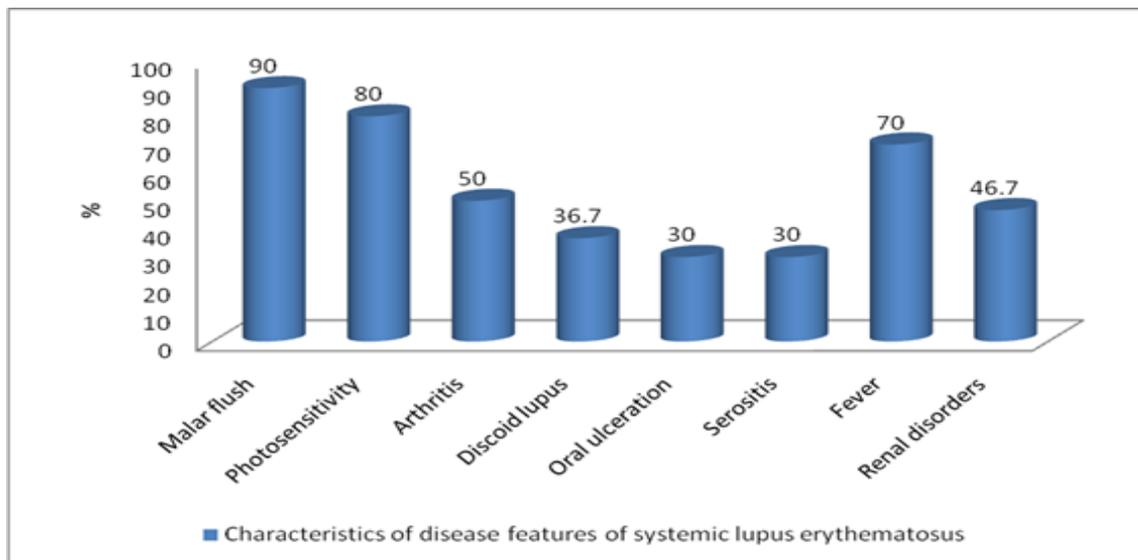


Figure (1): Characteristic of the disease features of the systemic lupus erythematosus

Table (2):Peripheral hemogram and acute phase reactants in patients with systemic lupus erythematosus (SLE)

Laboratory variables	SLE(N=30)
Red blood corpuscles (RBCs) 10^{12} /dL (mean \pm SD)	3.35 \pm 0.19
White blood cells (WBCs) 10^9 /dL (mean \pm SD)	5.69 \pm 0.81
Platelets (PLT) 10^9 /dL (mean \pm SD)	273 \pm 25.4
Hemoglobin (Hb) g/dL (mean \pm SD)	9.2 \pm 0.59
Erythrocyte sedimentation rate (ESR) 1hour mm/h (mean \pm SD)	74.3 \pm 6.63
ESR 2hours mm/h (mean \pm SD)	121.4 \pm 5.26
C-reactive protein (CRP) mg/L (mean \pm SD)	20 \pm 6.7

Table (2) clears the peripheral hemogram and acute phase reactants in patients with SLE. All mean values of peripheral hemogram are normal except hemoglobin level was below normal (9.2 \pm 0.59 g/dL). On the other hand all mean values of acute phase reactants are above normal; ESR at 1st and 2nd hour (74.3 \pm 6.6 and 121.4 \pm 5.26 mm/h, respectively) and CRP(20 \pm 6.7 mg/L).

Table (3): Thyroid function test values in patients with Systemic lupus erythematosus (SLE)

Thyroid function test (normal range)	No. of observed	Range of observed values	Mean \pm SD
F T ₃ (82-179ng/dL)	30	41.9-277	136.6 \pm 14.1
F T ₄ (4.5-12.5 μ g/dL)	30	0.8-18.3	8.83 \pm 1.2
TSH (0.4-4 μ IU/mL)	30	0.01-21	4.15 \pm 1.27
TG Ab(2-50 ng/mL)	30	0.0-255.7	15.12 \pm 11.15
Anti TPO[Anti thyro-peroxidase]Ab(up to 35IU/mL)	30	0.5-1001	121 \pm 65.4

Table (3) illustrates the thyroid function test values in patients with SLE. The table shows that range and mean \pm SD values of free T₃ in all patients are between 41.9 and 277ng/dL and mean of 136.6 \pm 14.1, free T₄ in all patients between 0.8 and 18.3ng/dL and mean of 8.83 \pm 1.2, TSH in all patients between 0.01 and 21ng/dL and mean of 4.15 \pm 1.27, TG Ab in all patients between 0.0 and 255.7ng/dL and mean of 15.12 \pm 11.15, and Anti TPO Ab in all patients between 0.5 and 1001 IU/mL and mean of 121 \pm 65.4.

Table (4):Positive RF, ANA, and thyroid auto-antibodies results in patients with systemic lupus erythematosus (SLE)

Variables	SLE (N=30)	
	No.	%
Rheumatoid factor (RF)	9	30.0
Anti nuclear antibody (ANA)	23	76.7
Thyroglobulin (TG) Ab	2	6.7
Anti thyro-peroxidase (TPO)Ab	5	16.7

Table (4) clarifies that 30.0% and 76.7% of SLE patients are positive for RF and ANA, respectively. Also, there are 6.7% and 16.7% of the patients' positive for TG Ab and anti TPO Ab, respectively.

Table (5): Results of thyroid function test in subgroups of patients with systemic lupus erythematosus (SLE)

Thyroid function subgroups	SLE (N=30)	
	No.	%
Normal thyroid function test	20	66.7
Abnormal thyroid function test	10	33.3
Subclinical hypothyroidism (normal FT ₃ , FT ₄ increased)	3	10.0
Biochemical hypothyroidism (normal or decreased FT ₃ decreased FT ₄ normal TSH)	2	6.6
Euthyroid sick syndrome (decreased FT ₃ normal or decreased FT ₄ normal TSH)	3	10.0
Biochemical hyperthyroidism (increased FT ₃ , FT ₄ and decreased TSH)	1	3.3
Subclinical hyperthyroidism (normal FT ₃ , FT ₄ and decreased TSH)	1	3.3

Table (5) reports distribution of the patients with SLE according to results of the thyroid function test. These subgroups are; normal thyroid function' group, 20 (66.7%) patients and abnormal thyroid function' group, 10 (33.3%) patients. The patients in the abnormal thyroid function group were 3 (10.0%) subclinical hypothyroidism, 2 (6.6%) biochemical hypothyroidism, 3 (10.0%) euthyroid sick syndrome, 1 (3.3%) subclinical hyperthyroidism, and 1 (3.3%) biochemical hyperthyroidism.

Table (6): Parameters of demographic, clinical, and laboratory data in patients with systemic lupus erythematosus (SLE) with normal and abnormal thyroid function

Parameters	Normal thyroid function	Abnormal thyroid function	FE t-test	P-value
	N=20	N=10		
	N (%) or (M± SD)	N (%) or (M± SD)		
Sex:				
Female	16 (80.0%)	8 (80.0%)		
Male	4 (20.0%)	2 (20.0%)	FE	1.0
Age (mean ± SD years)	37.5 ± 2.39	30.2 ± 3.81	5.539	0.999
SLE duration (mean ± SD month)	14.0 ± 2.21	4.9 ± 2.23	10.568	1.0
Hemoglobin (g/ dL)	11.37 ± 0.49	11.1 ± 2.34	0.361	0.64
RBC 10 ¹² /dL	4.12 ± 0.162	4.3 ± 1.3	-0.436	0.337
WBC 10 ⁹ /dL	7.4 ± 0.66	5.7 ± 1.72	3.016	0.992
PLT 10 ⁹ /dL	330.7 ± 22.3	257.1 ± 40.4	5.367	0.999
ESR 1 mm/h	76.5 ± 6.55	116.3 ± 11.34	-10.275	0.000
ESR 2 mm/h	100.8 ± 5.15	137.6 ± 8.4	12.71	0.000
RF	3 (15.0%)	6 (60.0%)	FE	0.03
ANA	13 (65.0%)	10 (100.0%)	FE	0.06
TG Ab	1 (5.0%)	1 (10.0%)	FE	1.0
AntiTPO Ab	1 (5.0%)	4 (40.0%)	FE	0.03

Table (6) clears different parameters of demographic, clinical, and laboratory data in SLE patients with normal and abnormal thyroid function. ESR at 1 & 2 hours, RF, and anti TPO Ab were the only laboratory results that showed statistically significant differences (P=0.00, 0.00, 0.03, and 0.03, respectively). On the other hand, the differences between SLE patients with- and without thyroid function test results; sex, age, duration of SLE, Hb, peripheral hemogram, ANA, and TG Ab were statistically insignificant.

Table (7): Different parameters of demographic, clinical, and laboratory data in systemic lupus erythematosus (SLE) patients with normal and subgroups of abnormal thyroid function

Parameters	Normal thyroid function	Hypo-thyroidism	Euthyroid syndrome	Hyper-thyroidism	* χ^2 **F-test	P-value
	N=20	N=5	N=3	2		
	N (%) or (M \pm SD)	N (%) or (M \pm SD)	N (%) or (M \pm SD)	N (%) or (M \pm SD)		
Sex:						
Female	16 (80.0%)	4 (80.0%)	2 (66.7%)	2 (100.0%)	0.833	0.841
Male	4 (20.0%)	1 (20.0%)	1 (33.3%)	0 (0.0%)		
Age (years)	37.5 \pm 2.39	29.6 \pm 4.18	29.75 \pm 4.3	30.8 \pm 0.3	15.634	0.000001
SLE duration/month	14.0 \pm 2.21	5.6 \pm 2.62	3.1 \pm 1.0	7.2 \pm 2.8	36.094	0.000
Hemoglobin (g/ dL)	11.37 \pm 0.49	13.4 \pm 1.63	7.87 \pm 1.12	12.47 \pm 2.16	23.12	0.000
RBC 10¹² dL	4.12 \pm 0.162	3.7 \pm 1.1	2.75 \pm 0.41	4.1 \pm 0.9	6.964	0.001
WBC 10⁹ /dL	7.4 \pm 0.66	7.4 \pm 1.28	4.8 \pm 1.02	6.2 \pm 0.8	9.724	0.0001
PLT 10⁹ dL	330.7 \pm 22.3	263.1 \pm 47.9	267.7 \pm 42.68	224.3 \pm 29.4	14.669	0.000001
ESR 1 mm/h	76.5 \pm 6.55	101.2 \pm 9.56	123.7 \pm 10.87	53.1 \pm 15.7	48.142	0.000
ESR 2 mm/h	100.8 \pm 5.15	126.8 \pm 7.9	140.2 \pm 7.53	88.4 \pm 27.2	36.035	0.000
RF	3(15.0%)	3 (60.0%)	2 (50%)	1 (50%)	1.534	0.674
ANA	13 (65.0%)	5 (100.0%)	3 (100%)	2 (100%)	4.565	0.206
TG Ab	1 (5.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	1.875	0.598
Anti TPOAb	1 (5.0%)	2 (40.0%)	1 (33.3%)	1 (50.0%)	6.12	0.1

Table (7) clarifies different parameters of demographic, clinical, and laboratory data in SLE patients with normal and subgroups of abnormal thyroid function. Age, SLE duration, Hb level, RBC, WBC, PLT, and ESR at 1 & 2 hours are the demographic, clinical, and laboratory results that showed statistically significant differences (P=0.00, 0.00, 0.00, 0.001, 0.0001, 0.00, 0.00, and 0.00, respectively). On the other hand, the differences between SLE patients without- and the subgroups with thyroid function test results; sex, RF, ANA, TG Ab, and anti TPO Ab were statistically insignificant.

DISCUSSION

The present work was conducted to study the thyroid dysfunction in SLE patients. Thirty patients from Internal Medicine and Rheumatology Departments known to have SLE were included in the study, their ages ranged between 17 and 37 years and the mean age was 26.1 \pm 1.5 year. Most (80.0%) of the patients were females. Our result regarding age is consistent with **Pradhan et al.** [16]; they found that SLE was diagnosed in age group 21-30 years. Also, **Zimmermann et al.** [17] cleared that at diagnosis, 24% of their SLE patients were under 20 years, 63% were between 20 and 40 years, and 13% were older than 40 years.

Further, according to **Tunbridge et al.** [18], the prevalence of subclinical hypothyroidism in females above the age of 18 was 7.5% and clinical hypothyroidism was 1%. Also, among 749 recorded cases of SLE during the period from 1989 to 2006. The average age at SLE onset was approximately 30.66 years [11]. Further, 100 patients with SLE, seen at the Department of Internal Medicine in Tunisia over a period between 1987 and 2001; the average age at the onset of disease was 32 year. Nineteen (19%) patients were aged over 50 years at the time of SLE diagnosis (late-onset SLE) [19].

As regard sex, SLE is an autoimmune disease affecting primarily women [2]. Our finding is agreement with **Houman et al.** [19]; they noticed that women were 92% and men 8%. Also, **Khanfir et al.** [11] showed that women were 90.3% and men were 9.7%, with an average age at SLE onset of approximately 30.66 years. Further, **Alarfaj et al.** [20] found that females were 90.7% among SLE patients' diagnosed with a mean age of 34.3 \pm 11.9 year and range 8-71 years.

At the same time, mean SLE duration was 9.3 \pm 5.3 year and range from 0.3 to 30 years [20]. Our short mean duration may be due to small number of our patients (30) compared with 624 patients in the study of **Alarfaj et al.** [20]. Also, it may be due to negligence of our SLE

patients in seeking medical advice due to socio-cultural and economic factors.

Regarding the most common characteristics of SLE features, they were malar flush (90.0%), photosensitivity (80.0%), fever (70.0%), arthritis (50.0%), and serositis (30.0%). **Borchers *et al.***^[2] stated that SLE is a systemic autoimmune disease with manifold clinical manifestations and immunological abnormalities. Our results were similar to **Houman *et al.***^[19]; they observed that among their SLE patients: 78% had articular-involvement, 53% photosensitivity, 63% malar rash, and 45% had serositis. Also, **Khanfir *et al.***^[11] showed that SLE patients were characterized by a high frequency of photosensitivity (67.6%), malar rash (68.7%), and renal involvement (49.5%). Further, they reported that nephritis was diagnosed in 43% of their cases and consisted always of glomerular nephritis, in three cases of which tubule-interstitial lesions were also observed^[19]. Also, neurologic involvement had prevalence from 8% to 32% of the patients according to their ethnicity. Serositis was present from 21% to 51% of the the patients according to their ethnicity. Vasculitis had an increased prevalence of 50%^[17].

Considering hematological characteristics of SLE patients; we noticed that their mean Hb level (9.2 ± 0.59 g/dL) was below normal value. Haematological abnormalities are common in SLE patients^[21]. Anemia is a common clinical finding in patients with SLE^[22]. It is found in about 50.0% of SLE patients^[21]. Further, anemia (Hb < 12 gm/dL) occurred in 63% of patients^[20]. Impaired erythropoietin response and presence of antibodies against erythropoietin may contribute to the pathogenesis of this type of anemia^[21]. In more details, **Alarfaj *et al.***^[20] found that 82.7% of SLE patients had hematological abnormalities at the time of diagnosis. WBC ($< 4 \times 10^9/L$) was present in 30%, lymphopenia ($> 1.5 \times 10^9/L$) in 40.3%, and platelets ($< 100 \times 10^9/L$) in 10.9%.

In the current study, we illustrated that the mean values of acute phase reactants were high; ESR at 1st and 2nd hour and CRP. These results may be due to that most of our cases had activity during time of the study. Also, SLE is a systemic inflammatory autoimmune disease as RA^[1].

Regarding thyroid function test results in patients with SLE; our data showed that the mean \pm SD values of FT₃ in all patients was 136.6 ± 14.1 ng/dL, FT₄ was 8.83 ± 1.2 ng/dL,

TSH was 4.15 ± 1.27 ng/dL, TG Ab was 15.12 ± 11.15 ng/dL, and anti TPO Ab in all patients was 121 ± 65.4 IU/mL. Thyroid dysfunction is frequent in SLE patients^[23]. Since symptoms of SLE and thyroid disease can be similar, so SLE patients should be routinely investigated for autoimmune thyroid disease^[7].

El-Sherif *et al.*^[24] showed that anti TPO Ab was found in 15% of SLE patients and 10% of controls. Also, anti TG Ab was found in 5% of SLE patients and 10% of controls.

Paul *et al.*^[1] showed that among the patients diagnosed with hypothyroidism and SLE, anti TPO Ab was positive in 72.7% ($P=0.037$). Also, they found 68.7% of patients with only SLE had anti TPO Ab positive, which was statistically significant ($P<0.05$). Further, **Kohno *et al.***^[25] found, in Japan, comparable results. However, these antibodies in SLE were often not thyroid specific^[1]. Monoclonal anti TPO Abs in these cases cross-react with lactoperoxidase, this is similar to human peroxidases such as TPO, neutrophil peroxidase, uterine peroxidase or myeloperoxidase^[25]. So, anti-TPO does not always correlate with the presence of thyroiditis in SLE^[1].

In the current study, we clarified that 30.0% and 76.7% of SLE patients were positive for RF and ANA, respectively. Also, 6.7% and 16.7% of SLE patients were positive for TG Ab and anti TPO Ab, respectively. One of the most common organs to be affected by organ-specific autoimmune injury is the thyroid gland. Whether concomitant organ-specific and systemic autoimmune diseases occur more often by chance than expected is a controversial issue. In particular, a large body of conflicting data has accumulated concerning the relationship between SLE and thyroid disease. Many studies and case reports have associated SLE with hypothyroidism, both subclinical and clinical forms^[1]. Positive RF was found significantly ($P=0.04$) more frequently found in SLE patients with autoimmune thyroid disease when compared with SLE patients without autoimmune thyroid disease **Appenzeller *et al.***^[7]. Anti nuclear antibodies (ANA) can be positive in a variety of conditions. It is also found in autoimmune thyroiditis^[26]. Further, ANA was present in all cases with SLE^[16]. Immunological features included ANA was observed in 100% of the patients^[19]. Also, ANA was present in 98.0% of SLE patients^[17].

In this study, we reported distribution of the patients with SLE according to their thyroid

dysfunction and thyroid function test results, 33.3% of SLE patients had abnormal thyroid function. Our result was lower than **El-Sherif et al.** [24]; they reported a high (50%) prevalence of thyroid disorders in SLE patients. On the other hand, our result was higher than that of **Zakeri and Sandooghi** [27]; they showed that 24.1% prevalence of thyroid disorders.

Our patients in the thyroid dysfunction group were 10.0% subclinical hypo-thyroidism, 6.6% biochemical hypothyroidism, 10.0% euthyroid sick syndrome, 3.3% subclinical hyperthyroidism, and 3.3% biochemical hyperthyroidism. The occurrence of hypothyroidism is common in SLE, a large body of data has support this [1]. Further, the presence of thyroid disorders is often correlated with SLEDAI (SLE disease activity index) [3]. Our results were comparable to **El-Sherif et al.** [24]; they observed that in their SLE group; 20% had hypothyroidism (10% subclinical and 10% biochemical), 20% had euthyroid sick syndrome, and 10% had hyperthyroidism (5% subclinical and 5% biochemical). Variable results were reported in many studies; prevalence of hypothyroidism and hyperthyroidism ranging from 3.9% to 39% and 0.0% to 10.9%, respectively [5, 1028,29]. These wide variations could be contributed to different sensitivities of the assay methods, the sample size included in the different studies, or racial prevalence of thyroid disease among the studied groups **El-Sherif et al.** [24]. Also, **Chan et al.** [30] noticed that 4.3% of their SLE patients had clinical hypothyroidism. **Mader et al.** [31] as well, cleared that 11.6% of their SLE patients had clinical hypothyroid compared to 1.9% in the control group.

Pyne and Isenberg [10] showed that prevalence of hypothyroidism in their SLE cohort was higher (5.7%) than in the normal population (1%), while that of hyperthyroidism (1.7%) was not significantly different.

Further, **Pan et al.** [14] cleared that 14% of the SLE cohort had thyroid antibodies, rising to 68% in the subgroup who also had thyroid disease ($P < 0.001$). Both antimicrosomal and anti TG Abs were detected. The antibodies were found in equally high frequency in the hyperthyroid subgroup (80% of patients), whereas in the hypothyroid subgroup antimicrosomal antibodies were more frequent than anti TG Abs (64% vs 41%). There was no significant difference in the frequency with which antimicrosomal or anti TG Abs were

detected between the hyperthyroid and hypothyroid subgroups ($P > 0.2$).

Also, **Miller et al.** [32] has noted a significantly higher than expected prevalence of hypothyroidism (6.6%) in SLE patients. Further, **ElSegai et al.** [15] reported that the overall thyroid dysfunction among SLE patients was 32.5% vs 12.6% in the control group ($P < 0.002$). The most prevalent thyroid dysfunction in SLE patients was subclinical hypothyroidism, 23.25% of patients whereas, in the control group subclinical hypothyroidism was present in 8.0% of patients, ($P < 0.002$). On the other hand, although subclinical hyperthyroidism was statistically insignificant in patients (9.3%) vs the corresponding group in control (4.7%), $P > 0.05$, and serum FT₄ was within the reference range, it was significantly higher than in control ($P < 0.01$). **Appenzeller et al.** [7] reported that symptomatic autoimmune thyroid disease was observed in 6.1% of SLE patients and in 2% of controls ($P > 0.05$), predominantly hypothyroidism 5.3% in SLE patients vs 2% in controls. Subclinical thyroid disease was identified in 11.5% and positive thyroid autoantibodies in the absence of thyroid disease in 17% of SLE patients. Thyroid autoantibodies preceded the occurrence of clinical autoimmune thyroid disease in 70% of SLE patients.

Disease activity of the SLE was correlated significantly with the presence of symptoms of hyperthyroidism [7].

CONCLUSION AND RECOMMENDATION

Thyroid disorders are common in SLE patients. The most common form is hypothyroidism. Patients with SLE should be evaluated for thyroid disorder by testing FT₃, FT₄, TSH, TG Ab, and anti TPO Ab for early detection of thyroid abnormalities. Further studies on large number of patients are needed to support and clarify the association between SLE and thyroid disorders in Egypt.

REFERENCES

1. **Paul R, Raychaudhuri P, Sinha PK et al. (2012):** Prevalence of systemic lupus erythematosus among patients of hypothyroidism in a tertiary care center. *Indian J Endocrinol Metab.*, 16(4): 569-74.
2. **Borchers AT, Naguwa SM, Shoenfeld Y and Gershwin ME (2010):** The geoeidemiology of systemic lupus erythematosus. *Autoimmune Rev.*, 9(5): A277-87.
3. **Bartels CM (2011):** Systemic lupus erythematosus. Available at: <http://emedicine.medscape.com/article/332244.overview#a0199>.

- 4. Kochupillai N (2000):** Clinical endocrinology in India. *Curr Sci.*, 79: 1061-7.
- 5. Weetman AP and Walport MJ (1987):** The association of autoimmune thyroiditis with systemic lupus erythematosus. *Rheumatology*, 26:359-61.
- 6. Dhir R, Ahluwalia AI, Sridhar Jet al. (2002):** Autoimmune thyroiditis predating the presentation of systemic lupus erythematosus: two cases and a review of literature. *Indian J Dermatol Venereol Leprol.*, 68: 292-4.
- 7. Appenzeller S, Pallone AT, Natalin RA and Costallat LT (2009):** Prevalence of thyroid dysfunction in systemic lupus erythematosus. *J Clin Rheumatol.*, 15(3):117-9.
- 8. Pearce EN, Farwell AP and Braverman LE (2003):** Current concepts: Thyroiditis. *N Engl J Med.*, 348:2646–55.
- 9. Brent GA, Larsen PR and Davies TF (2008):** Hypothyroidism and Thyroiditis. In: Kronenberg HM, Melmed S, Polonsky KS, Larsen PR, editors. *William's Textbook of Endocrinology*. 11th ed. Philadelphia: Saunders.
- 10. Pyne D and Isenberg DA (2002):** Autoimmune thyroid disease in systemic lupus erythematosus. *Ann Rheum Dis.*, 61:70–2.
- 11. Khanfir MS, Houman MH, Cherif E et al. (2013):** TULUP (TUnisian LUPus): a multicentric study of systemic lupus erythematosus in Tunisia. *Int J Rheum Dis.*, 16(5):539-46.
- 12. Latif S, Jamal A, Memon I, Yasmeen S, Tresa V, and Shaikh S (2010):** Multiple autoimmune syndrome: Hashimoto's thyroiditis, coeliac disease and systemic lupus erythematosus (SLE). *J Pak Med Assoc.*, 60:863-5.
- 13. Tektonidou M (2010):** Antiphospholipid syndrome. *Orphanet encyclopedia*, Available at: <https://rarediseases.info.nih.gov/diseases/5824/antiphospholipid-syndrome/cases/23207>
- 14. Pan X-F, Gu J-Q and Shan Z-Y (2015):** Patients with systemic lupus erythematosus have higher prevalence of thyroid autoantibodies: a systematic review and meta-analysis. *PLOS ONE*.
- 15. ElSegai OA-M, Farid EM and Ebrahim RA (2013):** Prevalence of thyroid dysfunction in systemic lupus erythematosus of Bahraini patients. *Bull Egypt Soc Physiol Sci.*, 33 (1): 123-9.
- 16. Pradhan V, Patwardhan M, Rajadhyaksha A et al. (2015):** Neuro-psychiatric manifestations and associated autoantibodies in systemic lupus erythematosus patients from Western India. *Rheumatol Int.*, 35(3): 541-5.
- 17. Zimmermann AF, deMessias IJ, Utiyama SR et al. (1997):** Clinical, autoimmune and demographic profile in systemic lupus erythematosus (SLE) patients from southern Brazil. *J Invest Allergol Clin Immunol.*, 7 (1): 24-31.
- 18. Tunbridge WM, Evered DC, Hall R, et al. (1977):** The spectrum of thyroid disease in the community: The Wickham survey. *Clin Endocrinol.*, 7 (6):481-93.
- 19. Houman MH, Khanfir SM, Ghorbell I and Miled M (2004):** Systemic lupus erythematosus in Tunisia: demographic and clinical analysis of 100 patients. *Lupus*, 13 (3): 204-11.
- 20. Alarfaj A, Aleem A and Khan N (2012):** Hematological abnormalities in 624 patients with systemic lupus erythematosus and their relationship with organ involvement. *Ann Rheum Dis.*, 71(3): 465-73.
- 21. Giannouli S, Voulgarelis M, Ziakas PD, and Tzioufas AG (2006):** Anaemia in systemic lupus erythematosus: from pathophysiology to clinical assessment. *Ann Rheum Dis.*, 65(2): 144-8.
- 22. Keeling DM and Isenberg DA (1993):** Haematological manifestations of systemic lupus erythematosus. *Blood Rev.*, 7: 199-207.
- 23. El-Saadany H, AbdElkhalik M, Moustafa T and Abd El bar E (2014):** Thyroid dysfunction in systemic lupus erythematosus and rheumatoid arthritis: Its impact as a cardiovascular risk factor. *Egyptian Rheumatologist*, 36: 71-8.
- 24. El-Sherif WT, ElGendi SS, Ashmawy MM et al. (2004):** Thyroid disorders and auto antibodies in systemic lupus erythematosus and rheumatoid arthritis patients. *Egypt J Immunol.*, 11(2): 81-90.
- 25. Kohno Y, Naito N, Saito K et al. (1989):** Anti-thyroid peroxidase antibody activity in sera of patients with systemic lupus erythematosus. *Clin Exp Immunol.*, 75:217-21.
- 26. Torok KS and Arkachaisri T (2010):** Autoimmune thyroiditis in antinuclear antibody positive children without rheumatologic disease. *Pediatr Rheumatol Online J.*, 8:15.
- 27. Zakeri Z and Sandooghi M (2010):** Thyroid disorder in systemic lupus erythematosus patients in Southeast Iran. *Shiraz E Med J.*, 11(1): 1-6.
- 28. Al-Saleh JA, El-Sayed ME, Jassim V et al. (2008):** Hypothyroidism determines the clinical and immunological manifestations of Arabs with lupus. *Lupus*, 17(3): 215-20.
- 29. Becker KL, Ferguson RH, McConahey WM (1983):** The connective tissue diseases and symptoms associated with Hashimoto's thyroiditis. *N Engl J Med.*, 268: 277-80.
- 30. Chan AT, Al-Saffar Z, Bucknall RC (2001):** Thyroid disease in systemic lupus erythematosus and rheumatoid arthritis. *Rheumatology*, 40(3): 353-354.
- 31. Mader R, Mishail S, Adawi M et al. (2007):** Thyroid dysfunction in systemic lupus erythematosus (SLE): relation to disease activity. *Clin Rheumatol.*, 26(11): 1891-4.
- 32. Miller FW, Moore GF, Weintraub BD, Steinberg AD (1987):** Prevalence of thyroid disease and abnormal thyroid function test results in patients with systemic lupus erythematosus. *Arthritis Rheum.*, 30:1124-31.