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ASSOCIATION OF THYROID DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Background: Systemic lupus erythematous (SLE) is a chronic autoimmune disease characterized by multisystem inflammation and presence of circulating auto-antibodies directed against self-antigens leading to inflammatory damage of many target organs including the skin, joints, kidney, blood-forming cells, blood vessels and the central nervous system**. Objective:** To assess the thyroid function status and to identify thyroid status in SLE patients. **Methodology:** This hospital based cross-sectional study was conducted at the Department of Medicine and Biochemistry in Sir Salimullah Medical College, Dhaka, during the period of January 2018 to December 2019. Adult patients with SLE were approached for inclusion in this study. Total 100 individual were interviewed focusing their socioeconomic status particularly family size and type, household income, years of formal education, occupation along with demographic profile. Moreover, clinical presentation, duration of disease, and severity were assessed. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was used to measure disease activity of the participants. Data collection were done by interviewing the patients and recorded in a separate case record form. Data analysis was done by the statistical program Statistical Package for Social Science (SPSS) version 25.0 (Chicago, Illinois, USA). **Results:** Among a total number of 50 SLE cases 82% were in euthyroid state, 8% had subclinical hypothyroidism, 6% had hypothyroidism and 4% patients had euthyroid sick syndrome. Among thyroid antibodies, anti-thyroid peroxidase (Anti-TPO) antibody was positive in 48% of SLE cases and anti-thyroglobulin (Anti-TG) antibody was positive in 32% patients. Thyroid disorder was present in 18% of SLE cases and all of them had positive anti-TPO antibody. **Conclusion**: It may be concluded from this study that thyroid disorders and presence of thyroid auto-antibodies are common in SLE patients and assessment of thyroid function in SLE patients as a part of biochemical and immunological profiles may help in early detection of associated thyroid disorders.

KEYWORDS: Systemic lupus erythematous, autoimmune, lymphocytes.

INTRODUCTION

SLE is an autoimmune disease that causes multiple organ inflammatory damage. It's often severe and can affect virtually all organs in the body.[1] Its diversity of clinical features is matched by the complexity of the factors (genetic, hormonal, and environmental) that cause it, and the array of autoantibodies with which it is associated.[2]

The Incidence of lupus is unknown, but varies by location and ethnicity. Lupus is characterized by production of auto-antibodies and polyclonal activation of B-lymphocytes that result in elevated immunoglobulin levels which also contribute to elevation of autoantibody level. Polyclonal activation by non-specific response to antigenic stimuli such as viral agents, or after loss of either B cell immune tolerance or suppressor T cell function to autoantigens may produce autoantibodies. Other mechanisms like defect in macrophage phagocytosis and production of immune complexes have also been described.[3] Various antibodies are found in SLE like ANA, anti-dsDNA, anti- Ro, anti-La, anti-Sm, anti-phospholipids antibody and others. The association between systemic lupus erythematosus (SLE) and thyroid abnormalities was first described in 1961 and showed that the presence of thyroid disturbance appeared to be more frequent in SLE patients than in the general population.[4] A study by Weetmen and Walport[5] has shown that 51% of SLE patients had thyroid antibodies compared to 27% of controls and elevated TSH were detected in 25% of SLE patients and 12.5% in the control group. Anti-thyroid antibodies were more frequent in SLE.[6]

The autoimmune process is thought to begin with the activation of CD4 + Thelper lymphocytes, which are specific for thyroid antigens. Activated CD4+T lymphocytes recruit cytotoxic (CD8+) T cells as well as B cells into the thyroid gland. Thyroid cell destruction

occurs through multiple mechanisms: cytotoxic T cells that induce apoptosis; cytotoxic antibodies that fix complement and cause thyroid cell lysis and antibody-dependent cell-mediated cytotoxicity (ADCC) involving natural killer cells. Subclinical hypothyroidism (SCH) is associated with a pro-atherogenic dyslipidemia and increased risk of cardiovascular disease.[7] These effects are being greater at higher TSH levels.[8]

MATERIALS AND METHODS

This hospital based cross-sectional study was conducted at the Department of Medicine and Biochemistry in Sir Salimullah Medical College, Dhaka, during the period of January 2018 to December 2019. A total number of 100 SLE patients were included. Data was collected through face to face interview with patients. Relevant clinical examination was done and evaluation included some laboratory investigations. These patients were diagnosed by using the American College of Rheumatology (ACR) criteria. Disease activity of SLE patients was recorded by using systemic lupus erythematous disease activity index (SLEDAI).[9] SLEDAI contains different parameters of disease. The serum was used for detection of thyroid hormone and auto antibodies. Total Tri-iodothyronine (T_3) was measured by radioimmunoassay kit (PR) IMK-422 imported from department of Isotope, China Institute of atomic Energy, Beijing. Total thyroxine (T_4) was measured by radioimmunoassay kit (PR) IMK-419 imported from Beijing Atom Hightech Co. Ltd, Beijing. TSH was measured by immune radiometric assay kit IMK-432 imported from Beijing Atom Hightech Co. Ltd, Beijing. Thyroid peroxidase (TPO) was measured by I-TPOAb radio immuno assay (RIA) kit IMK-417. Thyroglobulin (anti-TG) was measured by radioimmunoassay (RIA) Kit-476. Thyroid function of all the patients were done in the same laboratory and in the same set up. After editing, the coded data were directly entered into the computer by using statistical package for social science (SPSS) software for window version 20.

RESULTS

Table 1: Sex Distribution of SLE Patients (n=100).

Parameter	Number	Percentage (%)	Male/Female ratio
Male	24	24	3:1
Female	76	76	

Table 2: ACR Criteria of SLE patients (n=100).

Criteria	Number of patients	Percentage (%)
Malar rash	16	16
Non-specific rash	74	74
Arthritis	46	46
Arthralgia	18	36
Serositis		
Ascites	9	18
Effusion	6	6
Oral ulcer	42	42
Photosensitivity	40	40
Neurological criteria		
Headache	16	16
Convulsion	6	6
Anemia Mild (8-10 gm/dl)) Moderate (6-8 gm/dl) Severe (<6gm/dl)	 44 42 8	 44 42 8
Leucopenia (<4000/cmm)	6	6
Thrombocytopenia (<100000/cmm)	4	4
Renal criteria RBC >5/HPF(hematuria	52	52
Urinary total protein(UTP) (>0.5 gm/day)	72	72
ANA positivity	98	98
Anti-dsDNA positive	88	88

Table 3: Laboratory Parameters (n=50).

Parameters	Mean(SD)
T_3 (ng/ml)	1.31 ±0.59
T_4 (ng/ml)	83.92±26.41
TSH (mIU/L)	4.24± 2.44
TPO Antibody (U/ml)	47.16±114.87
TG Antibody (%)	22.11±24.96

Table 4: Thyroid Disorders among SLE Patients (n=100).

	Number of patients	Percentage
Hypothyroidism	6	6
Subclinical Hypothyroidism	8	8
Euthyroid Sick Syndrome	4	4
Euthyroid Patients	82	82

Table 5: Laboratory Data in Relation to Thyroid function (n=10).

Laboratory Data	SLE with Euthyroid function (n=82) Mean (SD)	SLE with Hypothyroidism (n=6) Mean (SD)	SLE with Subclinical Hypothyroidism (n=12) Mean (SD)	P value
SLEDAI Score	16.9±7.6	20.0±7.5	19.8±6.7	0.265
T_3 (ng/ml)	1.4 ±0.6	0.8 ±0.2	1.27±0.5	0.360
T_4 (ng/ml)	88.9±25.2	42.6±6.4	62.84±11.5	0.006
TSH (mIU/L)	2.0 ±1.4	8.9±2.4	5.6±0.3	0.001
Anti-TPO (U/ml)	34.4±99.7	262.5±199.3	21.4±7.2	0.006
Anti TG(%)	18.2±23.3	121.9±23.3	14.9±26.9	0.008

DISCUSSION

This study was designed as a cross sectional study to evaluate the the thyroid function status and to identify thyroid status in SLE patients. The present study findings were discussed and compared with previously published relevant studies.

This study shows among the 100 cases of SLE enrolled in this study, 76 were female and 24 were male, male: female ratio was 3:1. It is well established that females are more affected than male.[1]

Autoimmune thyroid disease is , which is characterized by the presence of autoantibodies to thyroid antigens and is associated with many non-organ-specific rheumatic diseases.[10,11]

In this study it was found that 6% SLE cases had hypothyroidism which is comparable to Miller et al.[12] where hypothyroidism was found to be as 6.6%, and Pyne and Ienberg[13] where it was found to be as 5.7% but higher than Kakehasi et al.[4] where it was found to be as 4% and less than Tsai et al.[10] where it was found to be as 8.8%, Park et al.[11] study where it was found to be 9.5% and Weetman and Walport[5] study where it was found to be as 24%. This variation in hypothyroidism may also be related to the patient's ethnic background, sample size, and sensitivity to enzyme-linked immunosorbent assay (ELISA) used to detect TSH levels.

Subclinical hypothyroidism was found in 8% SLE patients which is comparable to 10% by Kakehasi et al.[4] 10% by El-Sharif et al.[14] but higher than Park et al.[11] study where sub clinical hypothyroidism was found to be in 1.6% among Korean adult SLE patients. However it was less than 39%, 13.7% and 12% by Miller et al.[12] Pyne et al. reported that the prevalence of subclinical hypothyroidism was more than hypothyroid cases and which is similar to our study where hypothyroidism was 6% and subclinical hypothyroidism was 8% among SLE patients. All the SLE cases with hypothyroidism and subclinical hypothyroidism had positive anti-TPO antibody in their plasma.

In this study 4% of the SLE patients had euthyroid sick syndrome but none of them were positive for thyroid antibodies. In contrast to our study, Al-Awaddhi et al.[15] and Kumar et al.[16] found higher frequencies of euthyroid sick syndrome among SLE patients. In this study, hyperthyroidism was not detected in anyone among the SLE patients as well as among the reference groups. Some studies suggested that there was no increase in prevalence of hyperthyroidism in SLE patients.[12]

Euthyroid sick syndrome was found to be in 4% of SLE study population, which is much lower 1% reported by Kakehasi et al.[4]

Mean value of anti-TPO and ant-TG antibody level were significantly higher in hypothyroid cases than euthyroid cases but low in subclinical hypothyroid cases than euthyroid case. It is to be mentioned here that we did not find any hyperthyroidism among our studied SLE patients like Tsai et al.[10] El-Ghoneimy et al.[17]

CONCLUSION

This study suggested that thyroid disorders were detected in SLE patients. Most of the patients with thyroid disorders had positive anti-thyroid antibodies. Hypothyroidism and subclinical hypothyroidism was found in 6% and 8% of SLE patients respectively. So, from this small study it may be concluded that thyroid disorders are common in SLE patients and assessment of thyroid function in SLE patients as a part of biochemical and immunological profiles may help in early detection of associated thyroid disorders.

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