Original Article

Thyroid disorders in systemic lupus erythematosus patients

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Abstract

Objective : Thyroid abnormalities appeared to be more frequent in SLE patients than in the general population. The objective of the study is to assess the thyroid function status and to identify thyroid status in SLE patients.

Methodology : Our study included 50 pediatric SLE patients from the General Medical Hospital, Dhaka from January 2014 to July, 2015. These patients were diagnosed by using the American College of Rheumatology (ACR) criteria, revised 1997, which contains four or more criteria at a time or serially. Disease activity of SLE patients was recorded by using systemic lupus erythematous disease activity index (SLEDAI).

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 in18% of SLE cases and all of them had positive anti-TPO antibody.

Conclusion : 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.

Key Words : Systemic lupus erythematosus(SLE), Thyroid disorder

Introduction

Systemic lupus erythematosus (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. SLE in children is generally more acute and severe and more widespread organ involvement than in adults[1]. Approximately 15 to 20 % of SLE cases begin before the age of 19 years.[2] The incidence of lupus is not known but varies by location & 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 nonspecific response to antigenic stimuli such as viral agents or following loss of either B-cell immune tolerance to self-antigens or suppressor T-cell function may produce autoantibody. 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-ds DNA, 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 Walport5 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

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frequent in SLE.[6] The autoimmune process is believed to begin with activation of CD4+T-helper lymphocytes 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]

Results

Table 1: ACR Criteria of SLE patients (n=50)

Criteria	Number of patients	Percentage (%)
Malar rash	8	16
Non-specific rash	37	74
Arthritis Arthralgia	23 18	46
Serositis Ascites Effusion	 9 3	 36 6
Oral ulcer	21	42
Photosensitivity Neurological criteria Headache Convulsion	20 8 3	40 16 6
Anemia Mild(8-10gm/dl) Moderate(6-gm/dl) Severe <6gm/dl)	 22 21 4	 44 42 8
Leucopenia(<4000/cmm)	3	6
Thrombocytopenia (<100000/cmm)	2	4
Renal criteria RBC> 5 / HPF (hematuria)	26	52
Urinary total protein (UTP) (>0.5 gm/day)		
ANA positivity	49	98
Anti-dsDNA positive	44	88

Methodology

This cross sectional analytic study was done at General Medical Hospital Dhaka from January 2014 to July 2015. A total 50 SLE patients who attended at hospital were included purposively. Data was collected through face to face interview. Relevant clinical examination was done and evaluation included some laboratory investigations. These patients were diagnosed by using the American College of Rheumatology (ACR) criteria, 1997 (revised) which contains four or more criteria at a time or serially. 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-iodo thyronine (T3) was measured by radio- immunoassay kit (PR) IMK- 422 imported from department of Isotope, China Institute of atomic Energy, Beijing. Total thyroxine (T4) 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 SPSS software for window version 18.

Table 2 : Laboratory Parameters (n=50)

Parameters	Mean(SD)
T3 (ng/ml)	1.3 ±0.58
T4 (ng/ml)	83.9±26.4
TSH (mlU/L)	4.2± 2.4
TPO Antibody (U/ml)	47.1±114.8
TG Antibody (%)	22.0±24.9

Table 3 : Thyroid Disorders among SLE Patients (n=50)

Thyroid Disorders	Number of patients	Percentage
Hypothyroidism	3	6
Subclinical Hypothyroidism	4	8
Euthyroid Sick Syndrome	2	4
Euthyroid	41	82

Table 4 : Sex Distribution of SLE Patients (n=50)

Parameter	Number	Percentage (%)	Male/ female ratio
Male	12	24	3:1
Female	38	76	

Discussion

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. Among the 50 cases of SLE enrolled in this study, 38 were female and 12 were male, male: female ratio was 3:1. It is well established that females are more affected than male.[1]

Table 5 : Laboratory Data in Relation to Thyroid function (n=50).

Laboratory Data	SLE with Euthyroid function (n=41)	SLE with Hypothyroidism (n=3)	SLE with Subclinical Hypothyroidism (n=6)	P value
SLEDAI Score Mean (SD)	16.9±7.6	20.0±7.5	19.8±6.7	0.265
T3 (ng/ml) Mean (SD)	1.4 ±0.6	0.8 ±0.2	1.27±0.5	0.360
T4 (ng/ml) Mean (SD)	88.9±25.2	42.6±6.4	62.84±11.5	0.006
TSH (mIU/L) Mean (SD)	2.0 ±1.4	8.9±2.4	5.6±0.3	0.001
Anti-TPO (U/ml) Mean (SD	34.4±99.7	262.5±199.3	21.4±7.2	0.006
Anti TG(%) Mean (SD)	18.2±23.3	121.9±23.3	14.9±26.9	0.008

Autoimmune thyroid disease is marked by the presence of auto-antibodies directed against thyroid antigens, has been associated with a number of non-organ specific rheumatic disorders.[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 of hypothyroidism may also be related to ethnic background of patients, sample size and the sensitivity of Enzyme linked Immunosorbent Assay (ELISA) used to detect TSH level.

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 may be mentioned here that any hyperthyroidism was not found among the present studied SLE patients like Tsai et al[10] & El-Ghoneimy et al.[17]

Conclusion

Present study demonstrated 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 as a part of biochemical and immunological profiles may help in early detection of associated thyroid disorders.

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