ORIGINAL ARTICLE https://doi.org/10.3329/jmcwh.v21i1.79873

THYROID DYSFUNCTION AND ITS ASSOCIATION WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is an autoimmune connective tissue disease of variable severity. Multisystem organ involvement and tissue damage in SLE is mediated by production of autoantibody, disposition of immune complex and abnormal activation of complement pathway. This study was designed to investigate the thyroid dysfunction and its association with active disease in patients with SLE. **Materials and Method**: This cross-sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2016 to June 2017. For this study, 30 SLE patients aged 18 to 55 years with duration of disease≤5 years were included. Thyroid function test was estimated. Z Proportion test and Binominal regression analysis were performed as applicable. *p* value <0.05 was accepted as level of significance. **Results:** In this study, median, interquartile range (IQR) TSH was 4.1 (2.4-7.4)μIU/L, FT_3 was 4.1 (3.0-4.5) pmol/Land FT_4 was 12.6 (8.2-14.0) pmol/L. About 26.7% patients had hypothyroidism and 6.7% had hyperthyroidism. Hypothyroidism was significantly (p=0.012) higher in active SLE and 2 times (95% CI: 1.317 to 3.037) more risk for development of active disease in SLE. **Conclusion:** This study concludes that hypothyroidism is more likely to occur in SLE patients. It is significantly associated with active SLE.

Keywords: Systemic lupus erythematosus (SLE), Thyroid dysfunction, Disease activity.

Cite this article: Abira M, Akhter QS, Islam MS, Islam S,Khan IS, Akter F, Ahmad R, Islam T. Thyroid dysfunction and its association with systemic lupus erythematosus. J Med Coll Women Hosp.2025; 21(1): 53-58. https://doi.org/10.3329/jmcwh.v21i1.79873

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystemic autoimmune connective tissue disease in which cells and organs undergo damage and initially mediated by tissue-binding auto-antibodies[1]. These antibodies form immune complexes which may play important role in formation of all clinical and laboratory manifestations[2]. Prevalence of SLE have shown unequal distribution among different countries of the world and also within the same country. The rates are estimated to be as high as 52 per 100,000 people in the United States and as low as 3 per 100,000 people in India[3]. Due to the improvement in diagnosis and treatment, the mortality rate of SLE has been greatly reduced. Yet, the mortality rate in SLE patients was still three times higher than that in the general population[4]. Autoimmune diseases may be divided into organ-specific and systemic. Tissue-binding auto-antibody and inflammatory cytokine frequently affect the thyroid gland causing destruction of thyroid follicular cells and leading to hypothyroidism[5,6].

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Due to common genetic and gender background, it is believed that hypothyroidism and SLE may occur together, but usually have their own characteristic clinical manifestations[5,6]. Few studies[4-6] have been executed on thyroid disease and SLE. However, there is paucity of data available on SLE and hypothyroidism in our setting. Therefore, present study was performed more comprehensively to investigate prevalence of thyroid disease in SLE patients and assess their association with active SLE.

MATERIALS AND METHOD

Setting and study participants

This cross-sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2016 to June 2017. A total 30 SLE patients diagnosed on the basis of American College of Rheumatology (ACR) criteria[1] with age ranging from 18 to 55 years with duration of disease≤5 years were enrolled from SLE clinic of Dhaka Medical College Hospital by purposive sampling method. Disease activity was assessed by using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score[7]. We categorized our respondents into 2 groups such as patients with active disease (score >9) and inactive disease (score ≤9). Sample size was calculated by a statistical formula. The patients having history of liver disease, renal disease (other than SLE), rheumatoid arthritis, inflammatory bowel disease, ankylosing spondylitis, psoriasis and malignant disease, recent history of blood transfusion and history of taking anticoagulant, chemotherapy were excluded from the study.

Procedure

After selection of the subjects informed written consent was taken and nature, purpose and benefit of the study were explained to the subject.

The research work was carried out after obtaining ethical clearance from Ethical Review Committee of Dhaka Medical College Dhaka. All the information was recorded in a prefixed data schedule. With all aseptic precautions, 3.6 ml blood was collected from all subjects. Thyroid function test (TSH, FT3 and FT4) was estimated by Automated Analyzer.

Statistical analysis

Data were expressed as median, interquartile range (IQR), frequency, percentage and mean ± SD. Z proportion test was performed to compare proportion between the groups. Binary logistic regression analysis was performed to calculate Odd Ratio (OR). 95% confident interval (CI) was calculated and p value <0.05 was accepted as level of significance. Statistical analyses were performed by using IBM SPSS (statistical package for social sciences) Statistics for Windows version 26.0.

RESULTS

In this study, median age of the SLE patients was 34.5 (26.7-44.2) years and majority (93.3%) were female (Table- 1). About 63.3% of the SLE patients had SLEDAI score >9 (active disease) (Figure-1). We observed that median (IQR) TSH was 4.1 (2.4-7.4) μIU/L, FT_3 was 4.1 (3.0-4.5) pmol/L and FT_4 was 12.6 (8.2-14.0) pmol/L (Figure-2). About 8 (26.7%) patients had hypothyroidism, 2(6.7%) had hyperthyroidism and 20 (66.7%) had euthyroid (Figure-3). We found that about 19 (63.3%) patients had active disease. Hypothyroidism was significantly (p=0.012) higher in active SLE (42.1%) than inactive SLE (Table-2). Forest plot showed hypothyroidism was 2 times (95% CI: 1.317 to 3.037) more risk for development of active disease in SLE (Figure-4).

Table 1 : General characteristics of the subjects (N=30)

Parameters	SLE patients
Age (years)	34.5 (26.7-44.2)
Gender (%)	
Male	2 (6.7%)
Female	28 (93.3%)
BMI (kg/m^2)	20.3 (20.1-21.7)

Data were expressed as median, interquartile range (IQR), frequency and %. SLE= Systemic lupus erythematosus, BMI= Body mass index, N= total number of subjects

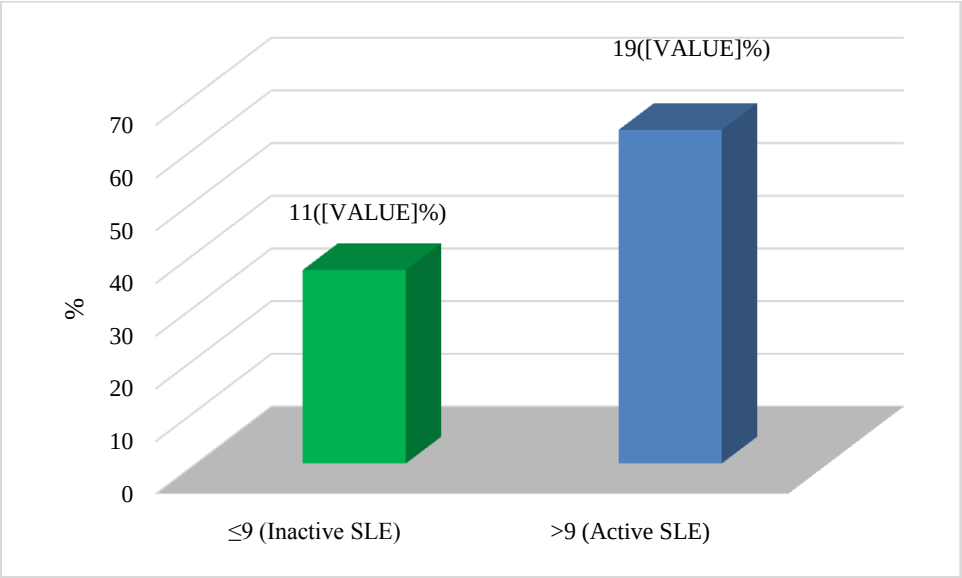


Figure 1 : Distribution of study subjects according to SLEDAI score presenting that majority (63.33%) of the SLE patients had SLEDAI score >9.

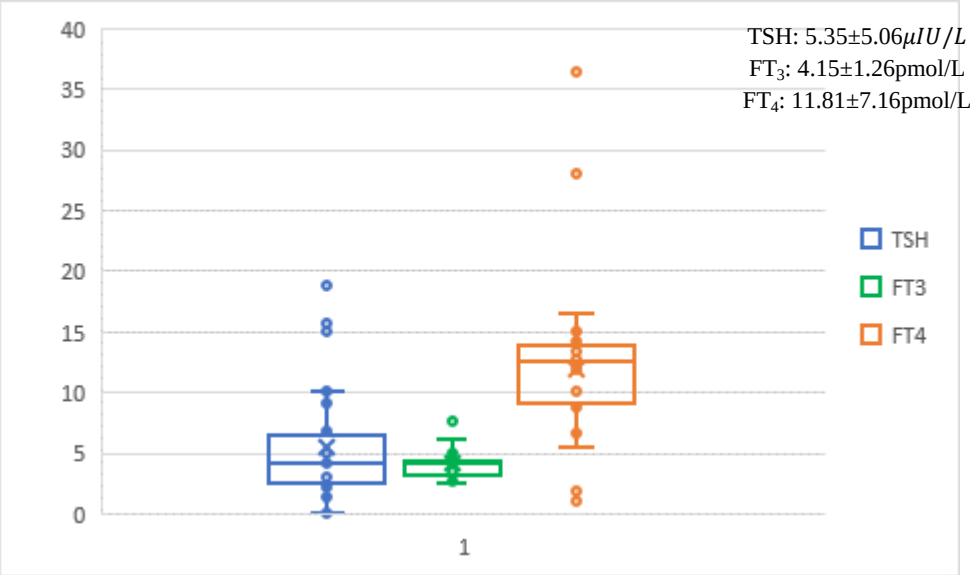


Figure 2 : Box and Whisker plot showed serum thyroid stimulating hormone (TSH), free triiodothyronine (FT_3) and free thyroxine (FT_4) levels of SLE patients.

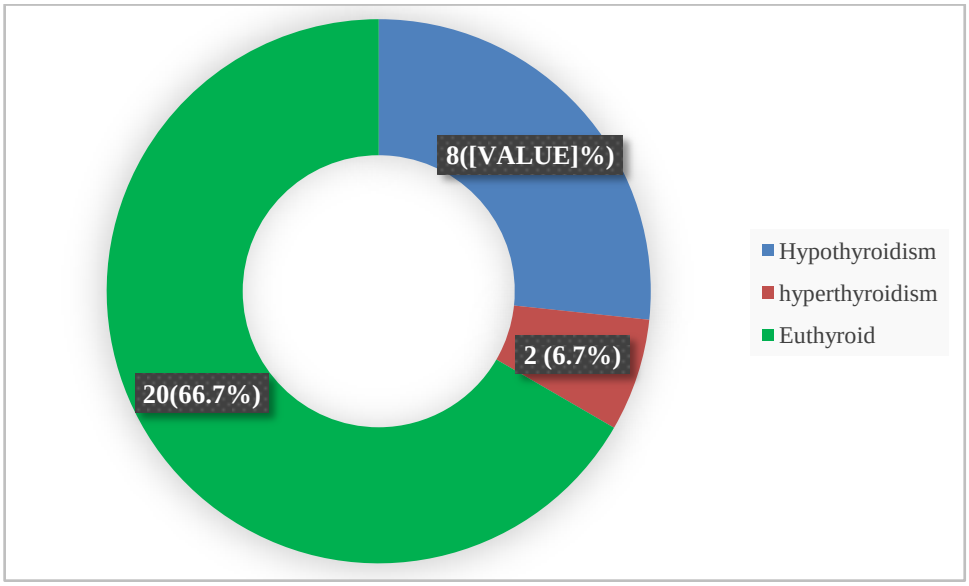
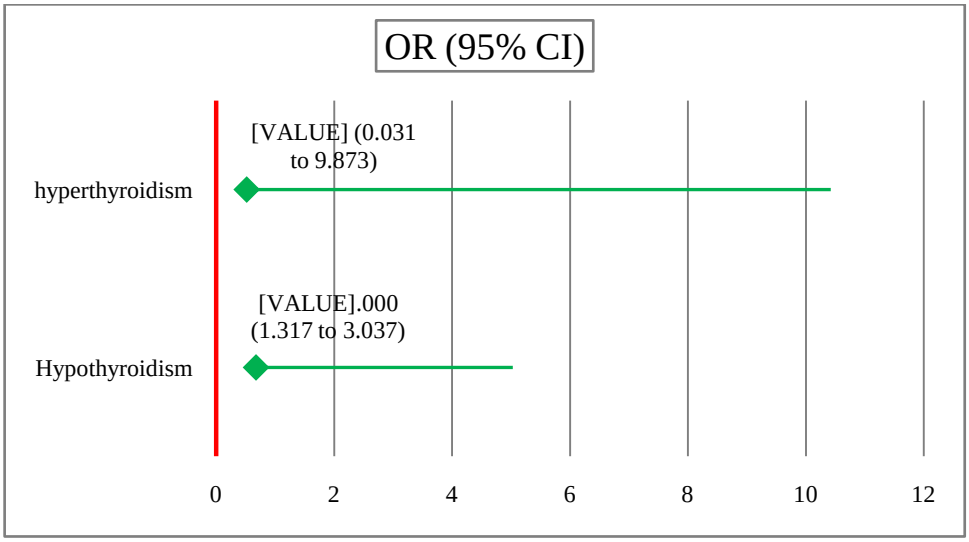


Figure 3: Distribution of study subjects according to pattern of thyroid dysfunction in SLE patients (N=30)

Table 2: Association of disease activity with thyroid dysfunction in SLE patients (N=30)

Thyroid status	Active SLE (n=19)	Inactive SLE (n=11)	*p* value
Hypothyroidism	8 (42.1%)	0 (0%)	0.012*
Hyperthyroidism	1 (5.3%)	1 (9.1%)	0.682
Euthyroid	10 (52.6%)	10 (90.9%)	0.032

Data were expressed as frequency (%). *p* value was obtained from Z-Proportion test.
*=significant



OR calculated from Binominal regression analysis.

Figure 4: Forest plot showed hypothyroidism was 2 times (95% CI: 1.317 to 3.037) more risk for development of active disease in SLE.

DISCUSSION

In current study, median (IQR) TSH was 4.1 (2.4-7.4) μIU/L, FT_3 was 4.1 (3.0-4.5) pmol/L and FT_4 was 12.6 (8.2-14.0) pmol/L. In Egypt, El-Baky et al.[8] performed a study and reported that mean ± SD of serum TSH, FT_3 and FT_4 levels were 7.685±10.172, 1.912±0.549 and 0.815±0.386 IU/L. About 26.7% patients had hypothyroidism and 6.7% had hyperthyroidism. Hypothyroidism was significantly (p=0.012) higher in active SLE than in case of inactive SLE. Mader et al.[9] observed that about 11.6% of SLE patients had hypothyroidism. None of them had hyperthyroidism. Yu-chuan et al.[10] executed a study in Taiwan and reported that SLE patients had significantly higher rate of hyperthyroidism and hypothyroidism. Athanassiou et al.[6] showed about 8.9% patients were found to suffer from primary hypothyroidism, 11.11% from subclinical hypothyroidism and 2.22% from hyperthyroidism.

In existing study, hypothyroidism was 2 times (95% CI: 1.317 to 3.037) more risk for development of active disease in SLE.As SLE is an autoimmune disease, therefore, autoimmunity has an important role in development of hypothyroidism in our study. Mader et al.[9]found no significant association between severity of disease with thyroid dysfunction in their study. Athanassiou et al.[6]also found significant association between SLE and thyroid disease.

Longo et al.[11] reported that genetic and environmental factors appear to contribute to the development of SLE. Interactions between susceptible genes and environmental factors result in activation of innate and adaptive immune pathways triggering lymphocytic infiltration of the thyroid gland which leads to destruction of the thyroid gland. Therefore, there is insufficient release of thyroxine, which causes hypothyroidism[5].

Pro-inflammatory cytokines are released in SLE during activation of immune cells. These cytokines (interferon) bind with its receptor on target cells and inhibit translation of mRNA. These autoimmune cytokines have important roles in destruction of thyroid follicular cells, leading to hypothyroidism[5,12].

CONCLUSION

Contemporary study revealed thyroid dysfunction is more frequent in SLE patients. Hypothyroidism is more likely to occur in SLE patients. It is evident that a significant association is observed between thyroid dysfunction and disease activity. It may influence the calculation of disease activity scoring. Therefore, thyroid function tests should be performed routinely in SLE patients and should be treated.

LIMITATIONS

Small sample size and single hospital-based study did not reflect exact situation of the whole SLE community. Even though biochemical hypothyroidism in these SLE patients were quite evident by testing free thyroxine and free triiodothyronine levels, the causes of hypothyroidism could not be confirmed by performing thyroid specific autoantibody testing due to time and financial constraint.

CONFLICT OF INTEREST

There is no conflict of interest.

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