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ORIGINAL ARTICLE

Thyroid dysfunction and anti-thyroid antibodies in Egyptian patients with systemic lupus erythematosus: Correlation with clinical musculoskeletal manifestations☆

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KEYWORDS

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Abstract *Aim of the work:* To study the prevalence of thyroid dysfunction and anti-thyroid antibodies (ATA) in Egyptian patients with systemic lupus erythematosus (SLE), and their association with musculoskeletal manifestations of the disease.

Patients and methods: Cross sectional study included 100 SLE patients and 100 matched controls. Clinical manifestations at any time during disease course were reported. Detailed musculoskeletal examination was done using Ritchie articular index (RAI), 44-Swollen joint count and fibromyalgic tender points. Phalen's test was used to diagnose carpal tunnel syndrome. Free-thyroid hormones (FT3 and FT4), thyroid stimulating hormone (TSH), anti-thyroglobulin (anti-TG) and anti-thyroid peroxidase (anti-TPO) antibodies were measured.

Results: The prevalence of thyroid dysfunction was significantly higher in patients than controls (18% vs. 4%, $p = 0.003$) and all were females. Prevalence of subclinical hypothyroidism (SCHT) and clinical hypothyroidism (CHT) is 10% ($p = 0.002$) and 4% ($p = 0.121$) versus non among controls while, that of subclinical hyperthyroidism (4%) was not significantly different. Prevalence of anti-TPO and anti-TG is higher in patients than controls (35% vs 11%, $p < 0.001$ and 22% vs. 6%, $p = 0.001$). All patients with SCHT had anti-TPO and half of them had anti-TG while all patients

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with CHT had both antibodies. Hypothyroidism was associated significantly with aging ($p = 0.01$), longer disease duration ($p < 0.001$), high BMI, high RAI scores, arthritis, positive Phalen's test and fibromyalgia ($p < 0.001$ for all) in comparison to euthyroid patients.

Conclusion: Hypothyroidism was more prevalent in SLE patients and its detection is recommended to reduce the risk of musculoskeletal related morbidity.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune, multifaceted inflammatory disease often associated with other organ-specific autoimmune diseases [1]. Autoimmune thyroiditis is an organ-specific disease and its association with thyroid dysfunction and SLE was reported in several studies and yielded conflicting conclusions. While some studies reported higher prevalence of hypothyroidism in SLE patients others reported higher prevalence of hyperthyroidism [2–8]. The association between thyroid dysfunction and SLE was first reported by White et al. [9] and Hijmans et al. [10] in 1961, who showed that the thyroid dysfunction appeared more common in SLE than in general population. Thyroid involvement being non-life-threatening than other organ involvement in SLE, it is often underestimated and passes undetected for long contributing to the morbidity of the illness. So, it is important to diagnose the thyroid dysfunction in lupus patients and to treat them accordingly [2]. The aim of this study was to estimate the prevalence of thyroid dysfunction and anti-thyroid antibodies in Egyptian SLE patients and their association with the musculoskeletal manifestations of the disease.

2. Patients and methods

2.1. Patients

A cross sectional case–control study included 100 Egyptian SLE patients who met the American College of Rheumatology Classification criteria of SLE [11,12] with age more than 18 and had at least 5-year disease duration and 100 age and sex matched apparently healthy individuals served as control. The patients were recruited from the Maadi Armed Force Hospital during the period from October 2011 till October 2012. Demographic data and clinical manifestations at any time during the disease course were reported for all patients. Patients with thyroid disease, thyroid medications or thyroidectomy were excluded from the study. All participants provided written informed consent prior to their inclusion. This study was approved by the local ethics committees and in accordance with the ethical standards laid down in the 1964 declaration of Helsinki.

Full history taking and clinical examination were done taking into consideration the symptoms and signs of thyroid dysfunctions. Detailed musculoskeletal examination was done. Assessment of joint tenderness was done using the Ritchie articular index (RAI), 53 joints in 26 units, graded according to tenderness on pressure (0 = no pain; 1 = patient complains of pain; 2 = patient complains of pain and winces; 3 = patient complains, winces, and withdraws; maximum score 78) [13]. Assessment of joint swelling was done using the 44-Swollen joint count [14]. Fibromyalgic tender points were scored for each patient [15]. Phalen's test was used to diagnose clinically the carpal tunnel syndrome. This test was considered positive if there were paraesthetic symptoms along the cutaneous distribution of median nerve after maintaining maximal wrist flexion for one minute [16].

2.2. Laboratory investigations

Routine laboratory investigations for patients with SLE were done including complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum alanine transaminase (ALT), aspartate transaminase (AST), creatinine, complete urine analysis, 24 h urinary proteins, C3 and C4, anti-nuclear antibody (ANA), and anti-double stranded DNA (anti-ds-DNA).

2.2.1. Thyroid hormones and thyroid stimulating hormone (TSH) measurements

The sera were examined for free triido thyronine (FT3), free thyroxine (FT4) and TSH by micro-particle enzyme immunoassay. The normal reference range for FT3 is 1.8–4.6 pg/ml, for FT4 is 1.0–1.8 ng/dl and for TSH is 0.3–4.2 μIU/ml according to Bemben et al. [17] and Bell et al. [18]. Elevated TSH with low thyroid hormones was categorized as clinical hypothyroid (CHT), while those with high TSH with normal thyroid hormones were considered as subclinical hypothyroid (SCHT). Similarly, low TSH with raised thyroid hormones and normal thyroid hormones was called clinical hyperthyroid and subclinical hyperthyroid, respectively [2].

2.2.2. Anti-thyroid antibodies (ATA) measurements

Serum anti-thyroglobulin antibodies (anti-TG) and anti-thyroid peroxidase antibodies (anti-TPO) were measured by immune-metric assays. Antibodies were considered positive if levels were >1 IU/ml for anti-TG and >50 IU/ml for anti-TPO.

Statistical analysis: Data entry, processing and statistical analysis were carried out using Statistical Package for the Social Sciences version 20 (SPSS Inc., USA). Data were reported as mean ± standard deviation (SD). Tests of significance (student *t*-test, Chi-square test with Fisher's exact test, and Yates correction were used when appropriate) were used to compare between different groups. *p* values <0.05 was considered to be statistically significant.