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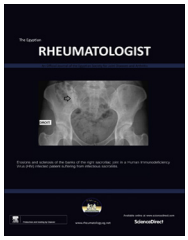

ORIGINAL ARTICLE

Thyroid dysfunction in systemic lupus erythematosus and rheumatoid arthritis: Its impact as a cardiovascular risk factor

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Abstract *Introduction:* Thyroid dysfunction and autoantibodies have been frequently associated with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

Aim of the work: To assess thyroid function and anti-thyroid antibodies in both diseases and elucidate the effects of the thyroid dysfunction on the clinical parameters, disease activity and cardiovascular risk.

Patients and methods: Forty SLE and forty RA female patients in addition to twenty controls were included. Free thyroxine (FT3), free triiodothyronine (FT4), thyroid stimulating hormone (TSH), anti-thyroid peroxidase antibodies (TPOabs), anti-thyroglobulin antibodies (TGabs), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and intima-media thickness (IMT) were measured. Disease activities were assessed in both diseases. In RA patients, the anti-cyclic citrullinated peptide (anti-CCP) was evaluated.

Results: A significantly higher TSH level was found in SLE patients compared to RA patients and controls. No significant difference was present between the RA patients and controls. Anti-TPOabs and anti-TGabs were more frequently detected in SLE (85% and 55%) compared to RA (50% and 37.5%). Abnormal thyroid function tests were detected in SLE, RA patients

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and controls in 52.5%, 17.5% and 10%, respectively. Subclinical hypothyroidism was the most common abnormality present followed by clinical hypothyroidism then euthyroid sick syndrome in both SLE and RA patients. A positive anti-CCP and high disease activity score (DAS28) in RA were among the strongest independent determinants of cardiovascular disease.

Conclusion: Thyroid dysfunction is frequent in SLE and RA patients. Those with thyroid dysfunction had increased cardiovascular risk.

1. Introduction

Autoimmune thyroid disease (AITD) is a term used to bring together a group of pathologies that has thyroid dysfunction and an autoimmune response against this endocrine organ, as its hallmark [1,2]. In an attempt to determine the genetic and environmental factors contributing to autoimmunity, clinical investigators have looked for relations between various autoimmune disorders such as rheumatoid arthritis (RA) [3], systemic lupus erythematosus (SLE) [4] Sjögren's syndrome [5], scleroderma, vasculitides, [6], alopecia areata [7] and AITD. In other words, AITD can be regarded as the most common autoimmune endocrinal disorders [1].

The prevalence of AITD in general population varies between countries. A prevalence has been described as 5–15% in women and 1–5%in male [8], meanwhile Helvaci et al. [9] reported that AITD affects about 2–4% of women and up to 1% of men worldwide, and the prevalence rate increases with advancing age.

Thyroid dysfunction is common in SLE and RA. Many are initially treated for thyroid dysfunction before the diagnosis of lupus or rheumatoid is made or vice versa [10]. Although the relationship between AITD and both SLE and RA has been revealed and blamed for precipitating or exacerbating their symptoms, the prevalence of thyroid disease is controversial and varied considerably [11]. The clinical presentation varies among those patients; it can be divided into those that cause clinical or subclinical hypothyroidism and hyperthyroidism [12].

Mousa et al. [13] found abnormal thyroid functions in 15.9% SLE and in 8.3% of RA patients and the most common abnormality was clinical hypothyroidism in 8.3% and 4.1% then subclinical hypothyroidism in 5.3% and 1.8% of the SLE and RA patients respectively. However, Assal et al. [14] reported that thyroid dysfunction was detected in 46.6% of SLE compared to 16.6% of RA patients and the most common abnormality was subclinical hypothyroidism followed by clinical hypothyroidism.

Autoimmune thyroid diseases are considered to be organ-specific. They are characterized by the presence of auto antibodies against thyroid specific components, such as thyroglobulin, thyroid peroxidase, and the thyrotropin (thyroid stimulating hormone; TSH) receptor which can either enhance or block the receptor activity [12]. However, although specific to AITD, anti-thyroglobulin (TGabs) [2] and anti-thyroperoxidase (TPOabs) [2] antibodies have been reported in many patients with nonthyroidal diseases, and even in the normal population [3]. On the other hand, a high prevalence of auto antibodies directed against nonthyroid-specific antigens has been described in patients with AITD [4,5]. These observations suggest that immune reaction of patients with organ-specific autoimmune diseases may be polyclonal organ and non organ-specific auto antigens [5].

Hollowell et al. [15] described a prevalence of 13% for TPOabs and 11% for TGabs among the general population. This prevalence rises spontaneously in hypothyroid patients. Appenzeller et al. [16] reported positive thyroid auto antibodies in the absence of thyroid disease in 17% SLE patients. [4] However, according to Mousa et al. [13] TPOabs were found in 19.7% SLE and 10.1% of the RA patients, while TGabs were found in 8.3% of the SLE and 6% of RA patients. Also Porkodi et al. [10] found TGabs positive in 82.4% in SLE and 56% in RA patients.

An accelerated progression of atherosclerosis in RA [17] and SLE [13] patients was already established than in healthy controls. Moreover SLE and RA patients with thyroid disorders are associated with enhanced risk of cardiovascular disease (CVD). There is evidence linking the patients with thyroid dysfunction especially hypothyroidism and the disturbance in the lipoprotein metabolism with a significant rise in the low density lipoprotein (LDL). The latter is the main responder in the development of atherosclerosis, formation of atheromatous plaques and enhancement of the cardiovascular risk [18].

However this is not totally explained with the low level of the thyroid hormone and the associated dyslipidemia, as restoration of the thyroid state does not influence the occurrence of the CVD [19]. These findings demonstrate the fact that the increased CVD in SLE and RA patients with thyroid dysfunction is complex and not fully clarified [18].

The aim of this study was to assess thyroid function and anti-thyroid antibodies in SLE and RA patients as well as to elucidate the possible effects of the thyroid dysfunction on the clinical parameters, disease activity and assess its impact as a cardiovascular risk factor.

2. Patients and methods

2.1. Patients

This study included forty SLE female patients aged from 20 to 41 years with a mean age of 28.4 ± 4.9 years, diagnosed according to the American College of Rheumatology Criteria (group I) [20], forty female RA patients aged from 23 to 46 years with a mean age of 29.1 ± 6.1 years diagnosed according to the 2010 ACR/EULAR classified criteria for RA [21] (group II). In addition, twenty age-matched healthy female volunteers served as controls (group III). Age of the controls ranged from 22 to 43 years with a mean value of 30.9 ± 4.8 years. They were recruited from the outpatient's