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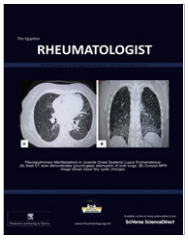

ORIGINAL ARTICLE

25-Hydroxy vitamin D levels and its relation to disease activity and cardiovascular risk factors in women with systemic lupus erythematosus

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KEYWORDS

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Abstract *Aim of the work:* To evaluate the associations of serum 25 hydroxy (OH) vitamin D [25(OH)D] levels with cardiovascular risk factors as well as disease activity in women with SLE.

Patients and methods: Fifty women with SLE as well as 30 controls were included in our study. Data collected included, demographics, SLE activity and damage assessments, cardiovascular risk factors, medications and laboratory assessment of inflammatory markers and 25(OH)D levels. Stepwise logistic regression analysis were used to estimate the association of 25(OH)D levels with cardiovascular risk factors.

Results: A significant lower 25(OH)D levels was found in SLE patients compared to controls ($P < 0.001$). A positive correlation was found between 25(OH)D and diastolic blood pressure, fasting blood sugar, cholesterol, triglycerides, LDL, BMI, as well as proteinuria and C3 levels. Furthermore, a significant positive correlation was found between 25(OH)D and the RT carotid artery

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stenosis and RT carotid artery plaque and the intima media thickness of both left and right carotid arteries. Lower 25(OH)D levels were also significantly associated with higher SLE disease activity and damage scores and steroid cumulative dose. Stepwise logistic regression analysis showed that higher BMI, diastolic blood pressure, cholesterol, triglycerides, LDL and diabetes mellitus act as predictors of lower 25(OH)D levels.

Conclusion: Our study found an association between lower 25(OH)D levels and increased cardiovascular disease (CVD) risk factors, as well as increased SLE disease activity and damage indices. Future studies are needed to determine relation of 25(OH)D and cardiovascular risk factors in patients with lupus.

1. Introduction

Several studies have suggested that 25-hydroxy vitamin 25(OH)D deficiency is an unrecognized contributor to the development of cardiovascular disease (CVD), cancer, and mortality. 1,25-Dihydroxy vitamin D affects the renin-angiotensin system [1], is associated with cardiac myocyte hypertrophy and has anti-inflammatory effects all of which may influence CVD risk [2]. Data from the third National Health and Nutrition Examination Survey (NHANES III) [3] found that adults with 25(OH)D levels <20 ng/ml compared with those with 25(OH)D levels $\geqslant 30$ ng/ml had an increased frequency of CVD, including coronary heart disease, heart failure, stroke, and peripheral arterial disease.

A leading cause of morbidity and mortality in women with SLE, including those who are premenopausal, is CVD [4] patients with lupus have an increased incidence of myocardial infarction up to 5 times that of the general population, with an age specific incidence in young women up to 50 times higher [5]. Evidence has been shown that like diabetes mellitus (DM), SLE itself is an independent risk factor for the development of atherosclerosis [6].

The identification of vitamin D receptor (VDR) in the cells involved in immune response and the discovery that activated dendritic cells produce vitamin D hormone suggested that vitamin D could exert immunoregulatory effects [7]. Vitamin D receptor is a member of the nuclear hormone receptor superfamily and has been identified in mononuclear cells, dendritic cells, antigen-presenting cells as well as activated T-B lymphocytes [8]. The effects of 1,25(OH)2D3 on the acquired, antigen-specific immune response is inhibition of both TH1and TH2 cell cytokine production, including IL-4, IL-6 [9,10], in addition vitamin D has been studied as a modifiable environmental factor [11] in autoimmune disease animal models, including SLE [12], experimental autoimmune encephalomyelitis [13], rheumatoid arthritis [14], type I DM [15] and inflammatory bowel disease [16]. SLE is the proto typical autoimmune disease and patients with SLE are known to have lower levels of 25(OH)D with measurements $\leqslant 20$ ng/ml [4] and in some cases, critically low at <10 ng/ml [17]. Lower levels of vitamin D have been shown to correlate with increased SLE disease activity [18] and studies using animal models of SLE demonstrated the attenuation of some manifestations with increasing vitamin D intake [3,12]. Our goal was to detect the association between 25-hydroxy vitamin D and cardiovascular risk factors in systemic lupus erythematosus patients and whether vitamin D levels are correlated with disease activity parameters.

2. Patients and methods

2.1. Study population

The study included 50 Egyptian SLE female patients with a mean age of 29.38 ± 9.2 years, fulfilling the 1982 revised criteria of the American Rheumatism Association for the classification of SLE [19], in addition to 30 healthy controls matched for age and sex with a mean age of 30.4 ± 7.1 years. All 50 patients and controls were premenopausal and were subjected to same sunlight exposure and clothing conditions. Three of the 50 SLE patients had history of cardiovascular accidents in the form of stroke which occurred in two patients and one patient developed myocardial infarction. All subjects were informed about the aim of the study and gave their consent. Patients were collected from the Rheumatology and Rehabilitation Department, Cairo and Fayoum University Hospitals.

2.2. Laboratory testing

Blood was drawn at the time of the study for analyses which included the following: antiphospholipid antibodies (aPL) (positive if IgG or IgM ACL was >40 IU/ml or if the lupus anticoagulants (“LAC”) was present. Antinuclear antibody testing (ANA), antiDNA using indirect immunofluorescence, C-reactive protein (CRP), serum complement (C3 and C4) levels by nephelometry and glomerular filtration rate were done to all patients. A complete blood picture, lipid profile, serum creatinine, liver function tests and electrolyte levels were tested for all enrolled cases.

25(OH)D levels was measured in the Department of Chemical Pathology, Cairo University Hospital by the 25(OH)D ^{125}I radioimmunoassay kit (Diasorin). The intra-assay coefficient of variation was 9.4%. Samples were measured in duplicate and the average value was reported. We defined vitamin D deficiency as <25 nmol/l while vitamin D insufficiency was between 25 and 75 nmol/l.

2.3. Traditional CVD risk factors

Information was obtained on age, smoking, diabetes, current estrogen use, current aspirin use, menopause status and history of cardiovascular disease (myocardial infarction, stroke, angina, transient ischemic attacks TIAs).

Systolic and diastolic blood pressure were determined using an average of 2 consecutive sittings 5 min apart. Blood