The impact of obesity on disease parameters ,quality of life ,functional capacity and risk of carotid arteries atherosclerotic plaque formation in Egyptian Systemic Lupus Erythematosus patients.

Thesis

Submitted in partial fulfillment of the master degree in Rheumatology and Rehabilitation.

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Abstract

This work aimed to study the effect of obesity on the quality of life , functional capacity and the risk of carotid atherosclerotic plaque formation in Egyptian Systemic Lupus Erythematosus patients and to correlate the findings with disease parameters .

Sixty patients with Systemic Lupus Erythematosus ,all fulfilling the 1997 revised criteria for the classification of Systemic Lupus Erythematosus.The patients were divided into three groups based upon body mass index (BMI,weight in kg /height in m^2)-BMI <25 (normal) ,BMI 25-29.99 (overweight) and BMI =30 (obese) .All patients included in this study were subjected to full history taking,clinical examination,laboratory investigations ,assessment of disease indices sa well as B mode carotid arteries ultrasonography.

In the present study there is an association between an increased BMI and increased lipid profile and also with decreased quality of life in Systemic Lupus Erythematosus patients and those with older age and increased waist circumference are at higher risk of premature atherosclerosis.

Key words : SLE-Obesity-Atherosclerosis.

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LIST OF ABBREVIATIONS

aCL : anticardiolipin antibodies .

ACLE : acute cutaneous lupus erythematosus.

ACR :American College of Rheumatology .

ANA :Antinuclear antibodies .

aPL :antiphospholipid antibodies .

APS :antiphospholipid syndrome .

AZA : Azathioprine .

beta2GPI : beta2-glycoprotein I .

BIA :Bioelectrical impedance analysis .

BILAG :The British Isles Lupus Assessment Group index.

BMI :Body Mass Index .

CBC :Complete blood count .

CFIDS :Chronic fatigue immune dysfunction syndrome .

CHD :Coronary heart disease .

CRP :C-reactive protein .

CCLE : Chronic cutaneous lupus erythematosus .

CAD :Coronary artery disease .

CVD :Cardio vascular disease .

DIL :Drug-induced lupus .

DLE :discoid lupus erythematosus .

DNA : Deoxy ribo nucleic acid .

dsDNA :Double strand deoxy ribo nucleic acid .

ECA :Endothelial cell activation .

ECM :Extracellular matrix .

ELISA :Enzyme-linked immunoassay .

ESR :Erythrocyte sedimentation rate .

FDA :food and drug administration .

FSS :Fatigue severity scale .

GIOP :Glucocorticoid-induced osteoporosis.

HAQ II :The Health Assessment Questionnaire II.

HDL :High-density lipoprotein .

HRQoL :Health-related quality of life .

IASO :International Association for the Study of Obesity .

IOTF :International Obesity Taskforce .

IL-1 :Interleukin-1.

IMT :Intima media thickness .

LDL :Low-density lipoprotein .

LN :Lupus nephritis.

MetS :Metabolic syndrome .

MRA :Magnetic resonance angiography .

MRI :Magnetic resonance image .

NAFLD :Nonalcoholic fatty liver disease .

NSAIDS :Non steroidal anti-inflammatory drugs .

OP :Osteoporosis .

p-ANCA :Perinuclear antineutrophil cytoplasmic antibody .

PDs : Psychiatric disorders .

PH : Pulmonary hypertension .

QoL :Quality of life .

RA : Rheumatoid Arthritis .

RNP :Ribonucleoprotein .

SCLE : Subacute cutaneous lupus erythematosus.

SES :Socioeconomic state.

SLAM :The Systemic Lupus Activity Measure.

SLE :Systemic Lupus Erythematosus.

SLEDAI :The Systemic Lupus Erythematosus Disease Activity Index.

SLICC :Systemic Lupus International Collaboration Clinics .

STAT4 : Signal transducers and activators of transcription-4.

TGs :Triglycerides .

TLR : Toll-like receptor.

TNF-α :Tumour necrosis factor-α .

TTP :Thrombotic thrombocytopenic purpura .

UV :Ultraviolet .

UVB : Ultraviolet B .

WHO : World health organization .

WHR :Waist-to-hip ratio .

Introduction

Recent epidemiological data demonstrate that the prevalence of obesity is beginning to plateau. However, the rate of severe obesity in adults and the prevalence of overweight among children continue to grow, suggesting that in the future there will be an increasing burden of obesity-related illnesses. Obesity is a very common chronic disease that poses significant health risks such as diabetes, cardiovascular diseases, hypertension and some autoimmune diseases ***(Bessesen, 2008).***

Both obesity and SLE have been found to have a component of inflammation as suggested by increased serum levels of tumor necrosis factor –α in SLE and by increased levels of interleukin-1 and c-reactive protein levels in both . Data from the Hopkins and Montreal General Hospital Lupus cohorts suggest that SLE patients have even a higher prevalence of obesity than individuals from the general population of their respective countries **(*Chaiamnuay et al.,2007).***

Adiposity may add to the inflammatory burden of SLE, thus contributing to cardiovascular disease risk ***(Marta et al.,2009).***Obesity especially in truncal distribution,is a risk factor for coronary heart disease events .In SLE ,obesity is frequently seen in truncal distribution and has been associated with the development of atheroma and coronary heart disease ***(Hirata et al.,2007).*** Accelerated atherosclerosis is considered as an important cause of morbidity and mortality in SLE patients,this role of atherosclerosis shows the importance of recognizing and controlling modifiable risk factors even in asymptomatic patients ***(Becker-merok,2009).***

Aim of the work

The aim of the present work is to study the effect of obesity on the quality of life , functional capacity and the risk of carotid atherosclerotic plaque formation in Egyptian Systemic Lupus Erythematosus patients and to correlate the findings with disease parameters .

Systemic Lupus Erythematosus

Introduction

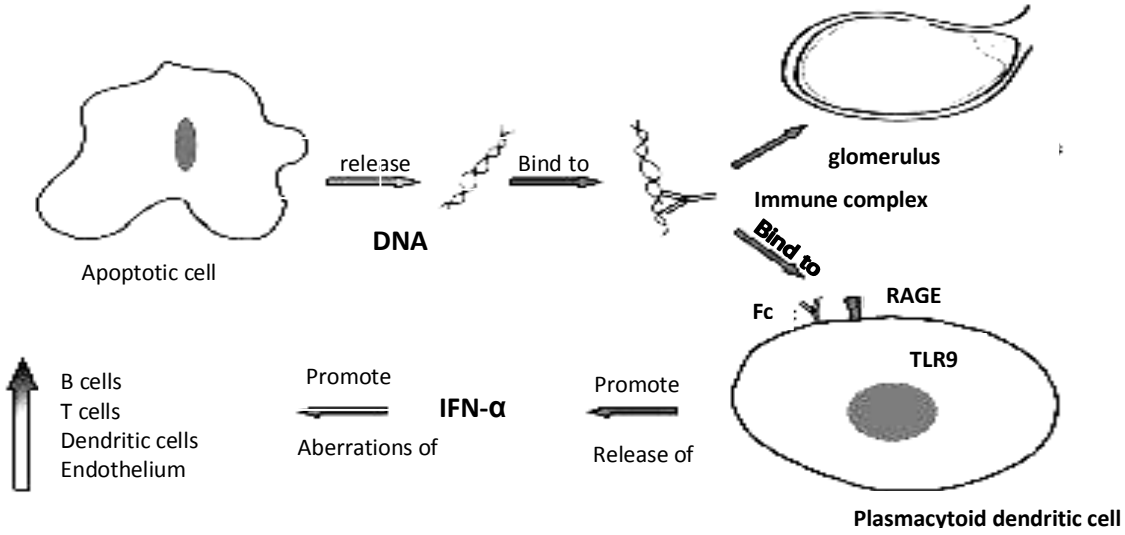
Systemic lupus erythematosus (SLE) is an organ non-specific complex autoimmune disorder, with multiple immunopathogenic mechanisms being implicated in its development. Loss of tolerance to nucleic acid antigens and other cross-reactive antigens is associated with the development of pathogenic autoantibodies that damage target organs, including the skin, joints, brain and kidney ***(Mohty ,2008).***

It is prevalent among young women with a peak age of onset between the late teens and early 40s and a female to male ratio of 9:1. It is more common in certain ethnic groups, such as people with African or Asian ancestry. ***(Gladman and Urowitz ,2007).***

Aetiology and pathogenesis

SLE is a prototype inflammatory autoimmune disease resulting from autoimmune responses against nuclear autoantigens. During apoptosis many lupus autoantigens congregate inside the cells and are susceptible to modifications . Modified nuclear constituents are considered foreign and dangerous. Therefore, apoptotic cells have to be efficiently removed to avoid the accumulation of apoptotic debris and the subsequent development of autoimmune responses. Hence, apoptosis and

clearance of apoptotic cells are considered key processes in the aetiology of SLE ***(Munoz et al ., 2008)***. Clearance deficiencies may account for the development of autoimmunity by inducing a loss of tolerance in lymphoid tissues. Furthermore, phagocytosis of apoptotic cells may lead to a pro-inflammatory response in the presence of autoantibodies. This may sustain inflammatory conditions and the pathology found in overt lupus ***(Pan and Sawalha.,2009).***



Fig(1): Model of key events in SLE pathogenesis (Ardoin and* Pisetsky *,2008)

(Dying cells release nucleic acid, includeng DNA, which binds immunoglobulin to form circulating immune complexes. These immune complexes can directly mediate cell damage by binding to target tissues, for example in the glomerulus. Immune complexes also bind Fc receptors on plasmacytoid dendritic cells, and in concert with receptor for advanced glycation end-products (RAGE) receptors and TLR9, promote expression and release of IFN-α. IFN-α, in turn, promotes multiple immune system aberrations including the upregulation of B cells, T cells, and dendritic and endothelial cells.)

{RAGE, receptor for advanced glycation end-products; TLR, Toll-like receptor :IFN,interferone}.

The clinical heterogeneity of this disease mirrors its complex aetiopathogenesis, which highlights the importance of genetic factors and individual susceptibility to environmental factors ***(Manson and Rahman , 2006).***

➡Genetic:

SLE is also complex genetically;although it runs in families, genes increase one's risk for SLE but do not fully determine the outcome. Interactions of multiple genes and/or interactions between genes and environmental factors are possible causes ***(Remmers et al .,2007).***

The concordance rate for lupus is 25% among monozygotic twins and approximately 2% among dizygotic twins; these rates indicate that a genetic contribution is important, but it is not sufficient to cause the disease. Many genes that probably contribute to SLE have been identified by means of whole-genome scans from families in which multiple members have lupus **(*Rhodes and Vyse ,2008)***.

The STAT4 gene (signal transducers and activators of transcription-4) , very recently identified as a SLE risk gene, predisposes specifically to severe manifestations of lupus, including kidney disease.Recently, a polymorphism of the STAT4 gene on chromosome 2q has been strongly implicated in the risk for development of SLE ***(Remmers et al .,2007).***