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Original Article

Metabolic syndrome in patients with systemic lupus erythematosus from South India

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ABSTRACT

Objectives: To find the prevalence of metabolic syndrome in systemic lupus erythematosus (SLE) compared to controls and to identify association of metabolic syndrome with SLE disease activity and damage.

Methods: A total of 82 SLE and 82 healthy controls were studied. Metabolic syndrome was defined by National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III), consensus definition for Asian Indian Adults and World Health Organisation (WHO) 1999 definition, and associations with lupus characteristics, disease activity, and damage were examined. Insulin resistance (IR) was estimated using the homeostasis model assessment for IR (HOMA-IR).

Results: Metabolic syndrome was present in 24.39% SLE and 12.19% controls ($p < 0.04$) by NCEP ATP III criteria; 29.26% SLE and 19.51% controls ($p = 0.14$) by consensus definition for Asian Indians; 18.2% SLE and 7.31% controls ($p < 0.035$) by WHO 1999 criteria.

Hypertension and hypertriglyceridemia were more frequent in SLE than in controls. Mean body mass index, diastolic and systolic blood pressure, triglycerides, and total cholesterol were higher in SLE than in controls. HOMA-IR (median, range) was 1.31 (0.06–9.32) and 1.55 (0.01–7.92), $p = 0.09$ in SLE and controls, respectively. There was no association of metabolic syndrome with disease activity/damage and prednisolone use. SLE patients with metabolic syndrome had a significantly longer duration of disease compared to patients without metabolic syndrome.

Conclusion: South Indian SLE patients have higher prevalence of NCEP ATP III and WHO defined metabolic syndrome compared to healthy controls. SLE patients have an altered lipid profile, but there was no IR and no association of metabolic syndrome with disease activity or damage.

1. Introduction

The prevalence of coronary heart disease (CHD) among patients with systemic lupus erythematosus (SLE) in the western population is 6–10%.[1–3] A seminal study by Manzi and colleagues on the cardiovascular events among SLE patients seen between 1980 and 1993 at their center showed that women with SLE aged 35–44 years were 50 fold more likely to develop CHD.[1]

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The role of metabolic syndrome in SLE is gaining attention, because it may contribute to this enhanced cardiovascular risk.[4] The metabolic syndrome is defined as a clustering of cardiovascular risk factors (central obesity, dyslipidemia, hypertension, and impaired glucose tolerance) in an individual which predisposes the person to a greater risk of developing type 2 diabetes and cardiovascular events.[5]

Up to 50% Asian Indian SLE patients have premature atherosclerosis in the form of significantly higher intima media thickness and plaques.[6] However, prevalence of metabolic syndrome in SLE in India has not been previously reported. Therefore, based on the reports of cardiovascular morbidity, premature atherosclerosis among SLE and high prevalence of the metabolic syndrome among Asian Indians,[7] we hypothesized that metabolic syndrome is not uncommon in SLE.

The objectives of this study were to find the prevalence of metabolic syndrome and its components in SLE patients, and to identify whether there is an association between metabolic syndrome with SLE disease activity and damage.

2. Materials and methods

We conducted a cross-sectional study on 82 SLE cases and 82 healthy controls in a tertiary care center located in South India from September 2012 to July 2013. The sample size was estimated to detect a minimum difference of 13% in prevalence of metabolic syndrome at 5% level of significance and 90% power.

Patients of SLE aged more than 18 years, who meet the updated 1997 American College of Rheumatology (ACR) classification criteria for SLE,[8] with disease duration of at least one year were included in the study. Patients were recruited from the Clinical Immunology outpatient and wards. Patients with diabetes at onset of SLE and patients with previous CHD (unstable angina, myocardial infarction) were excluded from the study.

Demographic details and information regarding age at onset of disease, duration of disease, and treatment received were collected. Every patient's case records were reviewed for lupus nephritis, vasculitis, hematologic manifestations, pericarditis, serositis, neuropsychiatric manifestations, and antiphospholipid syndrome (APS).

SLE disease activity was measured using Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI 2K),[9] and SLE disease damage was measured using the Systemic Lupus International Collaborating Clinics (SLICC) Damage Index.[10]

Age- and sex-matched healthy volunteers were invited to participate in the study, which comprised unrelated healthy attendants/visitors and healthy people identified from community camps. All the control subjects were healthy and none of them had any medical or surgical illness.

Physical examination included measurement of height in centimeters (cm), weight in kilogram (kg), and body mass index (BMI). Waist circumference (WC) measurements were obtained using nonstretchable flexible tape, just above iliac crest at end of normal expiration with subject standing erect and looking straight forward and observer sitting in front of the subject.[11] Blood pressure (BP) was recorded as a mean of two measurements obtained five minutes apart.

Informed consent was obtained from all study participants, and the study protocol was approved by the institute ethics committee.

2.1. *Biochemical assays*

Venous blood was obtained after eight hours of overnight fasting. Serum total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL) were estimated by enzymatic method using colorimetry. Two milliliters (ml) serum sample was stored at −80 °C for serum insulin. Fasting serum insulin was estimated by chemiluminiscence method (AVDIA Centaur Insulin Assay, Siemens Healthcare diagnostics). Ninety-five percent of values were in the range of 3–25 mU/L.

Insulin resistance (IR) was estimated using the homeostasis model assessment for IR (HOMA-IR) which was calculated as the product of fasting serum insulin (mU/L) and fasting plasma glucose (mg/dL) divided by 405.[12] Since there are no accepted cut off values of HOMA to define IR, we used 2.29 as abnormal value in our study, as has been previously described from a study in India.[13]

Participants (SLE cases and controls) were classified for the presence or absence of metabolic syndrome by National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III), the consensus definition for Asian Indians and World Health Organisation (WHO) 1999 definition.

The National cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III) defines the metabolic syndrome as being present, if three or more of the following five criteria are fulfilled[14]:

1. Central obesity – WC of >102 cm in men and >88 cm in women.
2. Hypertriglyceridemia; serum TG of >150 mg/dL.
3. Low HDL i.e., HDL-C <40 mg/dL in men and <50 mg/dL in women.
4. Hypertension – BP ≥130/≥85 mm Hg or use of drugs for high BP.
5. Fasting blood glucose >100 mg/dL.

Consensus definition for Asian Indians Adults is essentially a modification of the NCEP ATP III definition.[11] The cut off for WC is >90 cm in men and >80 cm in women. The remaining parameters are similar to the NCEP ATP III definition. Definition of metabolic syndrome by the consensus definition for Asian Indian adults includes any three of the following parameters:

1. Central obesity: WC >90 cm in men and >80 cm in women.
2. Hypertriglyceridemia; serum TG >150 mg/dL.
3. HDL-C <40 mg/dL in men and <50 mg/dL in women.
4. Hypertension – BP ≥130/≥85 mm Hg or use of drugs for high BP.
5. Dysglycemia – Fasting blood glucose >100 mg/dL.

WHO 1999 definition of the metabolic syndrome requires the presence of IR defined by any of the following three criteria: