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Original Article

A cross-sectional study to assess the association of systemic lupus erythematsous disease activity with levels of high sensitivity C-reactive protein

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ARTICLE INFO

Article history:
Received 6 March 2012
Accepted 2 March 2013
Available online 14 March 2013

Keywords:
SLE
SLEDAI
hsCRP

ABSTRACT

Background: Earlier studies have shown that active systemic lupus erythematosus (SLE), though an inflammation, is not associated with high C-reactive protein (CRP) levels. But a few recent studies have shown that high sensitivity CRP (hsCRP) may be elevated in SLE and is associated with organ damage.

Objective: To evaluate the association between hsCRP levels and SLE disease activity index (SLEDAI).

Methods: This cross-sectional study was conducted in 40 SLE patients. The SLEDAI was calculated and the hsCRP level was measured in the serum. Correlation between hsCRP levels and SLEDAI was assessed. Relationship of hsCRP levels with individual components of SLEDAI was also analyzed.

Results: Out of 40 patients, 38 (95%) were female. The mean age was 28.15 years. The mean SLEDAI was 27.4 ± 17.8, indicating that most of the patients had high disease activity. The mean hsCRP levels were 6.64 ± 5.09 mg/L. hsCRP levels and SLEDAI showed strong positive correlation (Pearson's correlation coefficient $r = 0.91$; $p < 0.0001$). hsCRP levels were higher in patients with serositis, nephritis, nervous system manifestations and immunological abnormalities.

Conclusion: hsCRP levels reflect SLE disease activity and are higher in patients with major organ involvement.

1. Introduction

Systemic lupus erythematosus (SLE) is a prototype systemic autoimmune disease. The etiology is unknown and the pathogenesis is complex. SLE is much more common in women than men. It may occur at any age, but occurs most often in between 10 and 50 years of age. SLE affects the skin, joints, kidneys, brain, and other organs. C-reactive protein (CRP) is a major acute-phase reactant produced in the liver in response to infection, inflammation, and trauma. Although CRP is

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0973-3698/$ – see front matter
http://dx.doi.org/10.1016/j.injr.2013.03.003

widely used as a marker of inflammation in various rheumatologic diseases, the biological function of CRP remains uncertain, particularly because it exerts both pro- or anti-inflammatory action depending on the level and type of Fcγ receptor expressed on cells at the site of CRP interaction.[1] Highly sensitive measurements of CRP can detect levels of 0.5–10.0 mg/L. This assay is referred to as high sensitivity C-reactive protein (hsCRP).

SLE is characterized by remissions and exacerbations. The increase in SLE disease activity is termed as flare, and is defined as an increase in SLE Disease Activity Index (SLEDAI) score of more than three from the previous SLEDAI score. There are different triggers for an SLE flare, and infections may also precipitate a lupus flare. A common clinical dilemma is to decide whether fever in a given case of SLE is due to lupus activity or infection, as therapeutic immunosuppression will be detrimental in the latter. C-reactive protein estimation may help in differentiating between the two. In contrast to other rheumatic diseases, SLE flare is found to be associated with low CRP respons whereas CRP rises during infection.

Although earlier studies have suggested that active SLE patients do not have elevated CRP levels.[2–4] Recent studies using hsCRP estimation have revealed that most SLE patients have elevated CRP levels during the disease process, irrespective of concomitant active infection.[5,6] Similarly, earlier investigators found no association between CRP levels and the patterns of organ involvement in SLE.[4,7] However, a few recent studies have shown an association between hsCRP levels and musculoskeletal, pulmonary and renal involvement in SLE.[5,6] There have been only a few studies looking at association of hsCRP with SLEDAI in the past. The present study focuses on the association of hsCRP with SLEDAI score, as well as the relation between hsCRP and organ system involvement based on components of SLEDAI.

2. Patients and methods

This cross-sectional study was conducted among patients attending the outpatient or in patient clinic of the Department of Medicine and Rheumatology of Medical College Kolkata. All newly diagnosed patients in the age group of 15–50 years, with SLE as per American College of Rheumatology, 1982 revised classification criteria,[7] were included in the study from June 2009 to November 2011. The exclusion criteria were: age less than 15 years or greater than 50 years, history of coronary artery disease, presence of active infection, impaired liver function (SGPT more than 90 IU/L), diabetes mellitus or presence of malignancy. Active infection was ruled out by history, clinical examination and routine investigations along with blood, sputum and urine culture. All patients gave informed consent. The clinical features, laboratory testing, and other data were recorded. The parameters studied included SLEDAI, hsCRP levels, Fasting blood sugar, complete blood count, liver and renal function test, 24-h urine protein, urine routine and microscopy, anti dsDNA, serum complement C3. hsCRP levels were analyzed with a Cobas Integra system (Roche diagnostics, Switzerland). The disease activity was assessed by SLEDAI.

Graph pad quick calcs software (graph pad software Inc, LaJolla, CA, USA), SPSS 20.0 and MS Excel 2007 were used for statistical analysis. Data were represented as mean ± standard deviation (SD) for continuous variables and as absolute numbers and percentages for discrete variables. Student *t*-test and Pearson's correlation coefficient were used for statistical analysis. A *p*-value of less than 0.05 was considered statistically significant. The study was approved by the Institutional Ethics Committee.

3. Results

A total of 62 patients were screened and ultimately 40 patients were enrolled in the study. We excluded 22 patients as 13 of them were having active infection, 4 had impaired liver function, 3 had impaired glucose tolerance and 1 each had coronary artery disease and lymphoma. Thirty-eight were females. The mean age was 28.15 (±8.86) years with a range from 15 to 50 years. The patients had a mean hemoglobin of 11.16 gm% (±1.96), and anemia was present in 21 (42%) patients. The mean ESR was 62 (±28.5) mm and all the patients had raised ESR. The average total leukocyte count was 7380 (±2653)/cu mm. Leukopenia was found in 5 (12.5%) patients. The mean platelet count was 196,650 (±95,720)/cu mm. The mean 24 h urine protein was 0.91 (±0.98) gm/24 h. Proteinuria was seen in 19 (47.5%) patients, 3 of them had nephrotic range proteinuria. Among other signs of SLE nephropathy, urinary cast was present in 22 (55%) patients, pyuria in 14 (35%) patients and hematuria in 16 (40%) patients. The mean SLEDAI score was 27.4 (±17.8) with 8 patients having SLEDAI less than 10. The mean hsCRP levels were 6.64 (±5.09) mg/L with 19 patients having CRP <6 mg/L and 9 patients having CRP >12 mg/L. There was a significant correlation between hsCRP and SLEDAI ($r = 0.91$, $p < 0.0001$; Fig. 1).

High sensitivity CRP values were different between patients with and without nephropathy, central nervous system involvement, hematological involvement, serositis and immunological parameters (Table 1).

4. Discussion

Our data showed increased levels of hsCRP in patients with SLE. This level correlated with disease activity. The level of

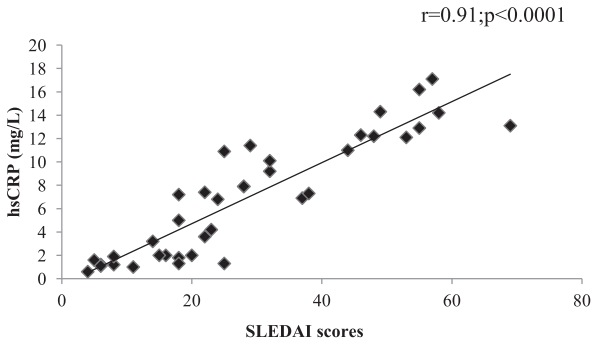

Fig. 1 – Scatter plot showing correlation between hsCRP levels and SLEDAI scores.