

Evaluation of anti-CCP in systemic lupus erythematosus patients in a referral center in Iran; A descriptive study

Mohammad Mehdi Emam¹, Mohammad Amin Shahrbafe², Maryam Hatam², Sina Asaadi³

1. Department of Rheumatology, Loghman Hakim hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Clinical Research Development Unit (CRDU), Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

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CORRESPONDING AUTHOR

Sina Asaadi
Loghman Hakim Hospital, Makhsoos St,
South Karegar Ave, Tehran.
Email: Dr.s.asaadi@sbmu.ac.ir
Tel: +982155419005

Background: Systemic lupus erythematosus (SLE) patients may have similar joint complaints in compare to rheumatoid arthritis (RA). In addition, some laboratory variables in both diseases may be associated with each other. It has been found that some patients with SLE may have anti-cyclic citrullinated peptide antibodies (anti-CCP) which is specific for RA; although, the clinical significance of such findings is not well established. This study aims to investigate the prevalence of anti-CCP in SLE patients in a referral center in Iran.

Materials and Methods: In this cross-sectional study that was done during a ten-year period in Loghman Hakim hospital, 784 SLE patients who had SLE criteria based on American College of Rheumatology guideline were entered to the study. Demographic features and the serum levels of anti-CCP were evaluated in all patients. Statistical analysis was done by version 16 of SPSS software.

Results: In this study, 11 male (9.6%) and 103 female (90.4%) who had SLE were included in the final analysis. The rate of SLE was higher in females. The mean age of patients was 40.2 ± 14.5 . Anti-CCP was positive in 20 of 114 SLE patients (17.5%). In addition, the rate of anti-CCP positive was higher in females (17 females in compare to 3 males).

Conclusion: It was concluded that approximately 20% of Iranian patients with SLE may have positive anti-CCP. However, careful and prolonged follow-up will reveal the real clinical value of anti-CCP in each patient individually.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disorder with various clinical and serologic findings. Early arthritis is a common presentation in SLE which can be similar to RA [1-3]. In the early presentations of SLE, it may be difficult to differentiate arthritis from RA; thus, some SLE patients may initially diagnosed with RA [4]. Some serum markers and laboratory findings including anti-nuclear antibodies (ANA) may be effective to differentiate SLE and RA; however, recent data have shown that ANA may be found in 10-70% of patients with RA [5, 6].

Anti-cyclic citrullinated peptide (CCP) antibody testing has

been used for the diagnosis of RA, with higher sensitivity and specificity than rheumatoid factor (RF) [7]. Considering 20 to 60% rate of rheumatoid factor (RF) positive in SLE patients, anti-CCP antibodies with 67-80% sensitivity have a higher specificity for RA (98-95%), and they can help diagnosis of possible rheumatologic diseases better than other antibodies [8-10].

Recently, it has been found that some patients with lupus may have anti-CCP antibodies; although, some controversies were observed in recent studies [11, 12]. Some studies suggested the association of anti-CCP it with arthritis and articular problems [13-15]; although, some other studies reject this relationship



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[16, 17]. Moreover, in many cases, positive level of anti-CCP antibody was associated with aggressive presentations, radiographic erosions and rhus syndrome (RA and SLE) [18-20]. The aim of this study was to determine the prevalence of anti-CCP antibodies in SLE patients in a referral center in Iran.

MATERIALS and METHODS

Study design

This descriptive, cross-sectional study was performed on patients with SLE disease during a three-year period in Loghman Hakim hospital, a referral center for rheumatologic disease in Tehran, capital of Iran. All patients who had SLE based on American College of Rheumatology criteria [21] and presented to the hospital from 2016 to 2019 were enrolled in the study. Convenience sampling was used for patient selection and patients who did not consent were excluded from the study.

Collecting data

After receiving the written consent from patients demographic information including age and gender were recorded from the patients. After that, 5 ml of venous blood was taken from each patient for measurement of anti-CCP and blood samples were collected in the laboratory of Loghman Hakim Hospital. Anti-CCP serum levels were measured by the QUANTA Lite™ CCP3 IgG ELISA kit (INOVA Diagnostics, Inc., San Diego, CA) and levels above 20 units per ml was considered as the positive level of anti-CCP antibodies in our study. All of the information was gathered in a questionnaire that designed by the researchers.

Statistical analysis

The collected data were analyzed for demographic characteristics and anti-CCP levels by version 16 of SPSS. The quantitative results were reported by mean and standard deviation (SD); moreover, the qualitative data were reported by number and percentage.

Ethical consideration

This study was conducted after obtaining permission from ethical committee of Shahid Beheshti University of Medical Sciences. All samples were entered voluntarily to the study and written consent was obtained from them.

RESULTS

In this study, 234 patients with SLE who were presented to the hospital during the study period which approximately 50% of them (n = 114) them were selected randomly. The mean age of the patients was 40.26 ± 14.54 years. Among these 114 patients, 11 were male (9.6%) and 103 were female (90.4%).

The results of the serum test for anti-CCP showed that 94 patients (82.5%) were anti-CCP negative. Statistical analysis of the patients with anti-CCP negative patients showed a mean age of 39.1 ± 14.55 . In addition, 8 men (8.5%) and 86 women (91.5%) were negative for anti-CCP. In patients with anti-CCP positive, the mean age of patients was 45.7 ± 13.4 years old and 3 men (15%) and 17 women (85%) were in this group. The results of study variables are presented in Table 1.

Table 1. The results of anti-CCP level based on the demographics

Variables	Anti-CCP level	
	Positive	Negative
Age	45.7 ± 13.4	39.1 ± 14.55
Gender	Male	3 (15%)
	Female	86 (91.5%)

DISCUSSION

In the present study, it was reported that approximately 20% of SLE patients may be positive for anti-CCP. In addition, the rate of anti-CCP positive in addition to the rate of SLE were higher in females rather than males. To the best of our knowledge, this study is the most recent study which evaluate the anti-CCP levels in SLE patients in Iran.

The anti-CCP that is found in SLE patients correlates with arthritis [22]. In fact, patients with erosive arthritis have a high titer of anti-CCP, which is not common in patients with SLE and is useful in identifying arthritis in SLE patients [23]. In addition, the erosive arthritis in the SLE may represent an overlapping between SLE and RA that referred as Rhus syndrome [24]. Several studies have shown that Anti-CCP in the serum of RA patients may occur over the years, with no clinical signs of the disease [25-27]. Additionally, the positive effects of both Anti-CCP and RF is associated with poor prognosis, and can increase the likelihood of RA detection by up to 100% [28].

The geographical and genetical backgrounds of the patients are some factors that associated with anti-CCP levels [29]. Moreover, the degree of joint involvement in patients (erosive or non-erosive) and the duration of the disease are some other factors that are associated with anti-CCP positive [30]. However, some studies suggested no significant relationship between the anti-CCP positivity and clinical features, including arthritis [16, 17]. Although, the population of the recent studies is low and the contradictory results can be due to the effect of this factor.

In this study, positive levels of anti-CCP was reported in 17.5% of patients.

Recent studies reported a range of 6.4-38% for anti-CCP positive in SLE patients [11, 12]. In the study of Faezi et al., the rate of anti-CCP positive was 4.7% in SLE patients with a high rate in patients with arthritis in compare to patients without arthritis [23]. In addition, in the study of Skare et al., the rate of anti-CCP was 13.7% in the Brazilian population [2]. Kakumanu et al. found that positive levels of anti-CCP may be observed in 17% of patients with SLE which is absolutely similar to the current study [15].

One of the limitations of this study is the lack of clarification of the clinical features of patients, such as the presence or absence of articular involvement and its relation with the degree of positive anti-CCP in these patients, which is recommended to note this point in future studies, furthermore, using statistical tests to examine the relationship between SLE and anti-CCP can be

more effective, this point can be considered in future studies.

CONCLUSION

This study suggests that anti-CCP testing in patients with SLE can be helpful in the diagnosis and treatment of these patients, especially in cases of articular involvement.

CONFLICT of INTREST

There are no conflicts of interest.

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