Original Article

Clinical Implications of the Presence of Anti-Ro Antibodies in Systemic Lupus Erythematosus in Sudan

Hassan A A Eltom[1], Hyder Osman Mirghani[2], Tayseer H Ali[3]
Abdelsalam Nail[4*]

Abstract:

Background: Ro- antigen is among many antigens that can be detected in SLE patients, with anti-Ro antibodies amounting to 90% in some patients. Although anti-Ro antibodies can be detected earlier than other antibodies, still their role is to be determined.

Aim: To estimate the occurrence of anti-Ro antibodies in patients with SLE, and its relation to classification criteria of the American College of Rheumatology (ACR) in Sudan.

Materials and Methods: Eighty- six patients with SLE, recruited from two rheumatology clinics in Omdurman- Sudan during the period November 2012 - May 2014. Participants gave consent then were interviewed for socio- demographic information and examined for skin, cardio-pulmonary, renal, neurological, and hematological manifestations to fulfill the ACR criteria for classification SLE. A Blood sample for full blood count, renal function, inflammatory markers, and antinuclear antibody profile including anti-Ro (SSA) was taken. This study was approved by the ethical committees of Omdurman and Military Teaching Hospitals. The Statistical Package for Social Sciences (SPSS) version 19 was used for data analysis. The Chi- square test was used for the relationship between categorical variables, and then Pearson's correlation was applied for different variables.

Results: Mean age was 36.4±11.6years, ranged from 18- 65 years. Female dominance is obvious (94.2%). Sixty six (76.7%) of subjects had arthritis, 45(52.3%) had oral or nasal ulcers, 35(40.7%) had malar rash, 31(36%) had photosensitive rash, while discoid rash was reported in 17(19.8%).

Twenty nine (33.7%) of SLE patients were positive for anti-Ro antibodies. The positive percentage was 100%, 50%, 45.8% and21.1% in patients with pericarditis, renal involvement, pleurisy and neuro-psychiatric manifestations respectively. While anti- Ro antibodies were detected in 35.9% of patients with positive anti- nuclear antibodies.

Conclusion: In the present study no association was found between anti-Ro antibody and the various manifestations of SLE. Larger multicenter studies are needed to assess the occurrence of anti-Ro antibodies in SLE, and their relationship with disease activity.

Keywords: Anti-Ro (SSA), SLE, ACR criteria.

Systemic lupus erythematosus (SLE) is a chronic remitting and relapsing auto-immune disease that can affect almost any organ in the body[1]. It usually affects young females, the cause is unknown but interaction of, genetic, environmental, and hormonal factors are blamed[2].

The outcome of this multi-organ disease varies according to race and gender. African Americans and those of lower education and socio-economic class had poorer clinical status including lupus nephropathy[3]. Although the incidence varies considerably, it is relatively more

1. Department of Internal Medicine, Faculty of Medicine, O.I.U, Omdurman, Sudan
2. Department of Internal Medicine, Faculty of Medicine, University of Tabuk, Tabuk, KSA
3. Department of Immunology, Omdurman Teaching Hospital, Omdurman, Sudan.
4. Department of Internal Medicine, College of Medicine, Aljouf University, Sakaka, Al-Jouf,KSA
*Correspondence to: Abdelsalam Nail
E-mail: abdelsalamnail@yahoo.com

common in Asians, and it is increasingly (the incidence is nearly tripled in the last 40 years of the previous century) detected due to improvement in diagnostic measures[4]. The American College of Rheumatology (ACR) criteriawere used for lupus diagnosis.

Ro- antigen is among many antigens that can be detected in SLE patients, with anti-Ro antibodies amounting to 90%in some patients [6]. Although anti-Ro antibodies can be detected earlier than other antibodies, and even before the diagnosis of SLE[7], still their role is to be determined.

Some previous studies suggest close correlation between anti-Ro antibodies and late onset SLE, with the onset of symptoms after the age of 50, but there is conflicting evidence between the correlation of anti-Ro antibodies and disease activity during the course of systemic lupus erythematosus[8].

In SLE anti-Ro antibodies have been reported to be associated with: photosensitivity, sub-acute cutaneous lupus erythematosus, cutaneous vasculitis (palpable purpura), hematological disorders, and interstitial pneumonitis, although no evidence of direct involvement of the antibodies in the pathogenesis of pulmonary disease, no erosive deforming arthritis, and passively transferred autoimmune disease that occurs in some babies born to mothers with anti-Ro antibodies[9, 10, 11, 12].

In the 1970s, due to the use of mouse tissue as a substrate for antinuclear antibodies (ANA) testing there were several reports of patients who met the American College of Rheumatology criteria for classification of SLE, but were persistently negative for ANA. By comparison, anti-Ro /SSA antibodies were found in most of these patients when a human cell line extract was used as the substrate for the Ro antigen[13].

As per our knowledge there are no studies that estimated the occurrence of anti-Ro antibodies in patients with SLE, and its relation to different components of the American Association of Rheumatology in Sudan. In the present research we studied the relationship of anti-Ro antibodies to different criteria of (ACR).

MATERIALS AND METHODS:

A total of 86 patients known to have systemic lupus erythematosus on medications (including disease modifying drugs), and regular follow-up, recruited from the rheumatic departments of Omdurman Teaching Hospital, and the Military Hospital during the period from November 2012 to May 2014. Children as well as patients with other connective tissue disorders were not included. Participants gave consent then interviewed and examined by the researcher. Information collected includes: socio-demographic, skin manifestations of lupus, cardio-pulmonary, renal, neurological, and hematological manifestations to fulfill the American College of Rheumatology Classification (ACR) criteria for systemic lupus erythematosus[5]. A Blood sample for full blood count, renal function, inflammatory markers, and antinuclear antibody profile was taken. Anti-Ro (SSA) was measured by Euroimmun Anti-Ro antibodies ELISA. This study was approved by the ethical committees of Omdurman Teaching and Military Hospitals. The Statistical Package for Social Sciences (SPSS) version 19 was used for data analysis. Descriptive analysis was done for all variables, then Chi-square test was applied for categorical data**,** and correlation was tested byPearson's correlation.

RESULTS:

Mean age of 86 patients was 36.4±11.6, ranged from 18- 65 years. Female dominance is obvious (94.2%). Sixty six

Table (1): The clinical and laboratory findings among the study group according to ACA criteria

Criterion	No (%)
Oral and/or nasal ulcers	45(52.3%)
Arthritis	66 (76.6%)
Photosensitive rash	31 (36%)
Discoid rash	17 (19.8%)
Malar rash	35 (40.7%)
Neuro-psychiatric disorders	19 (22.1%)
Renal involvement	14 (16.3%)
Pericarditis	2(2.3%)
Pleurisy	24 (27.9%)
Antinuclear antibodies	64 (74%)
Hematological manifestations	
Anemia	28 (32.6%)
Leucopenia	11 (12.8%)
Thrombocytopenia	5 (5.8%)
Immunological phenomena	
dsDNA	31 (36%)
Anti-phospholipids antibodies	9 (10.5%)
Anti-Smith (SM) Antibodies	12 (14%)
Anti-Ro antibodies	29 (33.7%)

Table (2): The prevalence of anti-Ro antibodies among patients in relation to ACA criteria

Criterion	No (%)	Anti-Ro positive
Oral and/or nasal ulcers	45(52.3%)	18 (40%)
Arthritis	66 (76.6%)	21(31.8%)
Photosensitive rash	31 (36%)	11 (35.5%)
Discoid rash	17 (19.8%)	8 (47.1%)
Malar rash	35 (40.7%)	15 (42.9%)
Neuro-psychiatric disorders	19 (22.1%)	4 (21.1%)
Renal involvement	14 (16.3%)	7 (50%)
Pericarditis	2 (2.3%)	2 (100%)
pleurisy	24 (27.9%)	11 (45.8%)
Antinuclear antibodies	64 (74%)	23 (35.9%)
Hematological manifestations		
Anemia	28 (32.6%)	10 (35.7%)
Leucopenia	11 (12.8%)	6 (54.5%)
Thrombocytopenia	5 (5.8%)	1 (20%)
Immunological phenomena		
dsDNA	31 (36%)	10 (32.3%)
Anti-phospholipids antibodies	9 (10.5%)	5 (55.6%)
Anti-Smith (SM) Antibodies	12 (14%)	3 (25%)

(76.7%) of subjects had arthritis, 45(52.3%) had oral or nasal ulcers, 35(40.7%) had malar rash, 31(36%) had photosensitive rash, while discoid rash was reported in 17(19.8%), Table (1) highlighted the (ARC) criteria of subjects. Twenty nine (33.7%) of SLE patients were positive for anti-Ro antibodies (all

females), almost 100% of patients with pericarditis had positive anti-Ro antibodies, 50% of those with renal involvement had positive antibodies, while 45.8% of patients with pleurisy had positive anti-Ro antibodies. Similarly 21.1% of patients with neuro-psychiatric manifestations showed positive antibodies, whereas anti- Ro antibodies was detected in 35.9% of patients with positiveanti-nuclear antibodies. Table (2) demonstrates the prevalence of anti-Ro antibodies among patients according to ARA criteria.

DISCUSSION:

It is suggested that anti-Ro antibodies are associated with late onset systemic lupus erythematosus with symptoms after the age of 50 years, there are conflicting data as to the correlation of these antibodies with disease activity during the course of SLE[6].

The mean age at diagnosis was 36.4±11.6 years similar to Kaballo *et al*[7], and Houman *et al*[8].

In the present study, female dominance is obvious (94.2%) with female/male ratio 16.2:1. Twenty nine (35.8%) of female were positive for anti-Ro antibodies, in accordance with previous studies[9, 10].

In the current study 33.7% of SLE patients were positive for anti-Ro antibodies, this result is lower than what is reported by Alarfag *et al*[11] in Saudi Arabia and Alsaleh *et al*[9] in United Arab Emirates who found that, anti-Ro antibodies were positive in 53.1% and 52.3% respectively, but is higher than what is reported by Kurien[12] where anti-Ro antibodies were present in 18.8% of lupus patients.The variation can be explained by the age, ethnicity, drugs, the method used to detect Anti-Ro, and fluctuation of anti-Ro antibodies through the course of the disease. In humans, a decrease in autoantibody titers has been shown during the course of MMF therapy[12].

In this study leucopenia was present in 54.5% of patients with anti-Ro positive SLE, in agreement with Kurien *et al*, who stated that neutropenia is present in 6/13 (46.1%) of anti-Ro positive SLE patients[13].

Our study demonstrated skin manifestations ranged from 35.5% - 47.1% of anti-Ro positive patients, and arthralgia was present in 31.8%. These results are in agreement with a study published by Popovic *et al*[14], which showed skin symptoms in 42%, and arthralgia in 31% of anti-Ro positive patients.

In the present study no correlation was found between anti-Ro antibody and the various manifestations of systemic lupus erythematosus, in agreement with Baptiste *et al*[15]. Additionally Hedpeth *et al* concluded that, no correlation between interstitial pneumonitis and anti-Ro antibodies in accordance with the present findings[16].

Our study is in contradiction with previous studies which showed correlation of anti-Ro antibodies with photosensitive rash [17], cutaneous vasculitis[18], and hematological disorders (anemia, neutropenia, and thrombocytopenia)[13].

Limitations of the study are the small size of the sample and it was conducted at two rheumatic centers, so generalization cannot be insured. Larger multicenter studies are needed to assess the occurrence of anti-Ro antibodies in systemic lupus erythematosus, and their relationship with disease activity in Sudan.

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