Comparison between the relationship serum levels of ANA Profiling panel antibodies and clinical symptoms in patients with systemic lupus erythematosus

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Abstract

Introduction: SLE is a chronic autoimmune rheumatic disease that is caused by autoantibodies and immune complexes for unknown reasons and causes damage to cells and organs. The aim of this study was to evaluate the association of ANA panel antibody with clinical manifestations in patients with SLE Methods: This retrospective cross-sectional study was performed on 110 patients with SLE. Clinical manifestations were evaluated according to ACR and SLICC criteria. In serum, the surface of ANA Profilling antibody was examined Results: There was no significant relationship between ANA profiling tests and disease manifestations. Except for the Anti-Ds DNA test, which was significantly associated with the clinical manifestations. ($P < 0.05$). The results obtained from the logistic regression model show that none of these variables age, sex, malar rash, discoid, oral ulcer, nephritis and arthritis have a significant effect on the outcome Anti-U1RNP / Sm (RNP / Sm), Anti-RO-52 recombinants, Anti-La / SS, Anti-SM not available ($P > 0.05$) Only age at onset has a significant effect on Anti SSA-Ro 60 (SSA) and Anti-Ds DNA tests. That is, on average, for each year of increasing the duration of the disease, the chance of a positive chance is about and about 16% increases for both tests. No significant correlation was observed with other test results at baseline. Conclusion: The present study shows an increase in the age of onset of the disease and also a decrease in the percentage of renal disorders compared to the study of the previous two decades in Iran.

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AbstractIntroduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune rheumatic disease thatis caused by autoantibodies and immune complexes forwithunknown reasons and causes damage to cells and organs. The aim of this study was to evaluate the association of ANAProfilingpanel antibody with clinical manifestations in patients with systemic lupus erythematosus.**Methods:** This retrospective cross-sectional study was performed on 110 patients (14 males and 96 females) with SLE. Clinical manifestations were assessed according to ACR and SLICC criteria. In serum, the surface of ANA Profilling antibodies was

examined by immunoblotting. **Results:** There was no significant relationship (chi-square test and Fisher's exact test) between ANA profiling tests and disease manifestations including maral rash, discoid, oral ulcer, nephritis and arthritis. Except for the Anti-Ds DNA test, which was significantly associated with the clinical manifestations of Maral Rush and Oral Ulcer. (P-Value <0.05). The results of logistic regression model show that none of these variables age, sex, malar rash, discoid, oral ulcer, nephritis and arthritis have a significant effect on the result Anti -U1RNP / Sm (RNP / Sm),RO-52 recombinant, Anti -La / SS , Anti-SM, do not have (P> 0.05). Only the age of onset of the disease has a significant effect on Anti SSA-Ro 60 (60kDa) (SSA) and Anti-Ds DNA tests on average, the chance of a positive test result increases by about 25% (P = 0.020 *, OR = 1.246, CI: 1.036-1.499) and increases by about 16% (P = 0.015 *, OR = 1.165, CI: 1.030-1.317) for both tests. There was no significant relationship between age of onset and other test results.**Conclusion:** The present study shows an increase in the age of onset of the disease and also a decrease in the percentage of renal disorders compared to the study of the previous two decades in Iran. Also, the significant relationship between Maral Rush and Oral Ulcer with Anti-Ds DNA's affinity is a confirmation of the results of extensive studies on this's affinity, which is also confirmed by the ACR criterion.

Keywords: Systemic lupus orthomatosis, ANA Profilling panel, imunoblottin

Introduction

Systemic lupus erythematosus (SLE) is a multisystem inflammatory disease of unknown etiology. Clinical signs and manifestations, laboratory signs, course and prognosis in patients vary and vary from patient to patient. Almost all organs of the human body are affected by the disease. In this disease, autoantibodies are produced against cell components and as a result, immunological reactions and inflammation caused by them cause cell and tissue damage in various systems. (1) These autoantibodies are not only diagnostically related. They may also relate to specific clinical subtypes (2) the American College of Rheumatology (ACR) revised criteria for SLE (3), as well as the latest classification of International Systemic Lupus Clinic Clinics (SLICC) in the diagnosis of SLE. Is used (4). The prevalence and incidence of SLE varies according to the population and the method used for diagnosis, but studies have shown that the incidence is 1 to 25 per 100,000 worldwide. Also, the reported prevalence of SLE in the United States is 20 to 150 cases per 100,000 people (5). In Iran, according to the latest studies, the prevalence of lupus is 40 per 100,000 people in urban society (6, 7). SLE can affect any organ and varies dramatically from patient to patient. Clinical manifestations are mainly a mixture of major skin, musculoskeletal, blood, serological, renal, or CNS complaints. The cause of SLE is still unknown but is likely to be multifactorial (8). Many studies have shown the role of genetic (9), hormonal (10), immunological (11) and environmental factors (12) in the pathogenesis of the disease. Due to the role of immune complexes in the pathogenesis of the disease, some of these antibodies are considered laboratory findings to meet the clinical criteria of SLE. Clinical manifestations and mortality in this disease or due to tissue damage caused by the disease itself and Or due to the side effects of various drugs used to treat lupus (13)

Immunogenetic mechanism of lupus disease

1. Tolerance to self-antigens is called self-tolerance, which is a feature of the natural and acquired immune system, the defect of which leads to immune reactions against insiders and autoimmune diseases, tolerance in both central and peripheral forms. And genes such as AIRE have an effect on this mechanism (14, 15)

2. CTLA-4 receptor binds to the B7 receptor on APCs, preventing it from binding to the CD28 stimulatory receptor and causing T lymphocyte energy. Studies show that CTLA4 is impaired in lupus patients. (14)

3. Th2 cells play an important role in the production of antibodies by acting on B lymphocytes. On the other hand, Th1 and Th2 cells have inhibitory and controlling effects on each other through the cytokines produced. Deviation and tendency towards (Th2 Skewing) has been observed in lupus patients which has increased the level of immunoglobulin and autoantibodies (16)

4. Any genetic disorder in the pathway of proteins of the internal and external pathways of apoptosis, such as a disorder in the Fas-FasL receptor that appears in the external pathway of apoptosis on T lymphocytes

and B lymphocytes, causes autoimmune diseases. (17)

5. BAFF (activating factor of B lymphocytes belonging to TNF family) is one of the effective factors in the preservation and survival of B lymphocytes and acts as a stimulator of B lymphocytes (BLYS) and can stimulate the BAFF receptor, causing more activity. B lymphocytes. In some patients with lupus, the level of BLYS is increased and its level is associated with an increase in Anti-ds DNA titer (18)

6. Regulation of hemoral immune responses using specific FcγIIB receptor on B lymphocytes as antibody feedback. Polymorphisms of this inhibitory receptor are associated with autoimmune diseases such as SLE. (19)

7. Genetic defects of several complement proteins such as C1q, C2, C4 cause autoimmune diseases such as SLE due to lack of clearance of immune complexes of circulating nuclear components and apoptotic components and their deposition in tissues and the development of type allergies II and III and tissue destruction (20)

Method

In this study, 110 people (14 men and 96 women) who referred to the rheumatology clinic of Imam Reza Hospital in Mashhad, Iran during 2020 and 2021, underwent a complete clinical examination and lupus was confirmed by two rheumatologists. Consent was obtained from patients to participate in the project. Other baseline information included age and time of onset of the disease and gender, which were collected as a checklist. The disease activity index was assessed according to ACR criteria in 1997 and the latest SLICC 2012 criteria. Clinical manifestations

including: arthritis, malar rash, subacute skin lupus or discoid, oral ulcers, renal disorders were collected in a questionnaire. Then, a total ANA test was performed on all patients by ELISA method and if this test was positive in the samples, the ANA profiling panel test was measured based on the Imonobloting technique based on the Euro Immun company kit.

Statistical analysis

Chi-square test was used and in cases where more than 20% of the expected frequencies of the tables were less than 5 (Cochran), Fisher's exact test (Fisher's Exact Test) was used. Logistic regression model has been used for general review. The software used in this study is SPSS v.26 and the significance level of the tests is less than 5%.

Results

The study group analyzed 110 patients (14 males and 96 females) with SLE, with a female-to-male ratio of 8.8 to 1.2, and a mean age of 38.63 years with a standard deviation of 10.15 (mean age in males and females 14, respectively). 36 years with standard deviation of 7.84 years and 38.99 years with standard deviation of 10.43 years) No statistically significant difference (Mann-Whitney test) was observed between the two groups (P = 0.317). The mean age of onset of disease in the studied patients was 32.57 years with a standard deviation of 10.92 (mean age of onset of disease in men and women was 27.43 years with a standard deviation of 10.87 years and 33.32 years with a standard deviation of 10.78), It was a year. There was no statistically significant difference (Mann-Whitney test) between the two groups (P = 0.054).

According to Table 1, the highest clinical manifestation was related to arthritis, in which 80 patients (72.7%) had this symptom, followed by Maral Rush with 60.9%, oral ulcer with 31.8, renal disorders with 13.6 and the lowest observed symptoms, respectively. It was discoid in which there were 5 patients (4.5%) and also according to Table 2, the highest prevalence of antibodies was related to Anti Ds-DNA test in which 52 patients (47.3%) were positive and the lowest was related to Jo-1 (Jo), PCNA (PCNA), Histones (H1) and Ribosomal-P-protein (RIB) in which only one person (0.9%) was positive. The results of the Scl-70 (Scl), PM-Scl 100 (PM100) and Centromere B (CB) tests were also negative. There was no significant relationship (chi-square test and Fisher's exact test) between age, onset age and sex with symptoms of Marar rash, discoid, oral ulcer, nephritis and arthritis. Only a significant correlation (Chi-square test) was observed between the

clinical manifestations of Marar rash and Oral Ulcer with the result of Anti-Ds DNA test (P-Value <0.05). The results obtained from the logistic regression model show that none of these variables age, sex, malar rash, discoid, oral ulcer, nephritis and arthritis have a significant effect on the result Anti -U1RNP / Sm (RNP / Sm) , Anti RO-52 recombinant , Anti -La / SS , Anti-SM do not have (P> 0.05). Only the age of onset of the disease has a significant effect on SSA-Ro 60 (60kDa) (SSA) and Anti-Ds DNA tests, namly on average, the chance of a positive test result increases by about 25% every year, respectively (P = 0.020 , OR = 1.246, CI: 1.036-1.499) and increases by about 16% (P = 0.015 , OR = 1.165, CI: 1.030-1.317) for both tests .There was no significant relationship between the age of onset and other test results

Table 1: Clinical features of 110 patients with SLE.

Clinical feature	n	Percentage
F/M	96/14	8.8/1.2
Arthritis	80	72.7
Malar rash	67	60.9
Oral ulcers	35	31.8
Nephritis	15	13.6
Discoid	5	4.5

Table 2 Immunological findings of 540 SLE patients

Anti Ds-DNA	52	47.3	Anti SSA-Ro 60 (60kDa) (SSA)	32	29.1	Anti-La/SS	19	17.3	Anti-SM 19 17.3 Anti -U

Discussion

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, a rheumatic disease with a non-transparent cause caused by autoantibodies and immune complexes that cause systemic damage. There are various reports from different countries of the world regarding the prevalence and characteristics of SLE. In these reports, the influence of genetic and environmental factors on the manifestations of SLE is discussed. In the present study, clinical and paraclinical characteristics (ANA Profilling panel) of 110 patients (14 Male and 96 female) with Iranian SLE have been studied. gnificant correlation was observed. an, as a country located in the Middle East and with the same race as the people of European countries, is a good candidate to study the effect of environmental and genetic factors on various manifestations of SLE. This disease is more common in women and in the present study 87.3% of female patients And 12.3% of the patients studied were men. The ratio of women to men was 8.8 to 1.2. The higher prevalence of the disease in women was reported in all studies, including the present study and studies in the region and European countries. In the region, the lowest ratio of women to men was reported in Lebanon (1.6 to 1) (21) and the highest in Kuwait (10 to 1) (22). In a study conducted by the Rheumatology Research Center of Tehran University of Medical Sciences from 1977 to 2011 on 2280 men and women with lupus, a male to female ratio of 9 to 1 was reported, which is consistent with our research (23). In our study, the mean age of all patients was 38.63 years with a standard deviation of 10.15 years. The mean age of men and women was 36.14 years with a standard deviation of 7.84 years and 38.99 years with a standard deviation of 10.43 years, respectively, and no statistically significant difference (Mann-Whitney test) was observed between the two groups (P = 0.317). The mean age of onset of the disease in the studied patients was 32.57 years with a standard deviation of 10.92 years. It should be noted that the mean duration of the disease was 6.05 years with a standard deviation of 4.82 years. The mean age of onset of disease in men and women was 27.43 years with a standard deviation of 10.87 years and 33.32 years with a standard deviation of 10.78 years, respectively, and no statistically significant difference (Mann-Whitney test) was observed between the two groups. P = 0.054). Compared to other studies, the age of onset was almost consistent. However, in the study of the Rheumatology Research Center of the University of Tehran, the mean age of onset was 24.4 ± 10.4, which is due to the increase in age of onset and alignment with European countries and the region. Better health care that has happened over a period of more than two decades (21, 22, 24, 25 and 26).

n this study, the highest clinical manifestations were related to arthritis in which 80 patients (72.7%) had this symptom. Malar rash with 60.9%, oral ulcer with 31.8%, renal involvement with 13.6 and the least observed symptoms were related to discoid. In which there were 5 patients (4.5%) in terms of the severity

of clinical manifestations according to the research of Rheumatology Research Center of Tehran University of Medical Sciences in which renal disorders with 65.4% most and then arthritis with 51.9, malar rash with 60, oral ulcers With 38.5, and the lowest percentage with discoid was 14.6. This is somewhat consistent with our study, except for renal impairment, which had the highest percentage in more than two decades ago, unlike our study, where arthritis was the most common complaint. The reason for this discrepancy may be the faster and more accurate diagnosis of lupus patients and more advanced treatments (23). A study by Cervera et al. In 2002 and 2006 on European populations found that arthritis had the highest at 48.1 percent, followed by maral rush at 31.3, renal impairment at 27.9, Olar ulcer at 12.5, and the lowest at 7.8 percent with discoid. . In similar studies conducted in several countries in the region, the percentage of skin manifestations (malar rash and discoid) in the countries of the region was in line with our research and doubled in European countries, since Iran is in a lower geographical orbit with ultraviolet rays. These results can be explained by the role of ultraviolet light in exacerbating skin manifestations (22, 24, 25, 26). In our view, the cumulative prevalence of ANA panel antibodies in SLE is limited to six more features searched. Anti-SmAnti Ds-DNA, Anti U1RNP / Sm, SSA Ro 60 Anti and La / SSB Anti, RO-52 recombinant were detectable in a recent study. Some research has been done to investigate the prevalence of these antibodies and clinical communication with very sensitive methods. In our study, based on immunoblotting, a relatively insensitive but highly specific method was used that allows you to identify antibodies to the ANA panel found in sera, Anti-Sm, Anti Ds-DNA, anti-U1RNP / Sm and Anti-La / SSB were frequent features in our group. They examined the clinical manifestations of confirmation of previous reports, and most of these associations continued after logistical analysis for all variables. No association was found between the symptoms of the disease including malaria, discoid, oral ulcer, nephritis and arthritis with ANA panel tests except for Anti Ds-DNA which is significantly associated with the clinical symptoms of oral ulcer and maral rash.in 2004 study by Forger et al. In the Department of Rheumatology at the University of Montserrat, Germany, on the clinical significance of anti-ds DNA isotypes in lupus nephritis showed a significant association with IgM isotypes and skin involvement and IgG isotypes. Nephritis has lupus erythematosus. And IgG / IgM ratio as a significant parameter for the diagnosis of lupus nephritis, which is consistent with our research (27) This was the first comprehensive report on the serum level of ANA panel antibodies in Iranian men and women with SLE. According to valid anti-SM reference values, it is found in only 30% of patients with lupus. However, due to its rarity in other rheumatic diseases such as rheumatoid arthritis, etc., it has significant diagnostic value. In the ACR classification criterion for SLE, it is considered as a pathway and has a value equivalent to Anti-dsDNA (28). In this study, Anti-SM with 17.3% was less than the reference value, which is probably due to the small sample size. In another study conducted in 2018 by Dr. Mir Amir Aghdashi et al. In the Rheumatology Department of Urmia University of Medical Sciences on 72 female patients with SLE on the level of Anti-SM antibody and clinical signs due to the small sample No significant relationship was found between clinical manifestations and Anti-SM antibody that is consistent with our study (29). We could not find an explanation for the significant age of onset of the disease on SSA-Ro 60 (60kDa) (SSA) and Anti-Ds DNA tests.

final conclusion

The present study shows an increase in the age of onset of the disease and also a decrease in the percentage of kidney disorders compared to the study of the previous two decades in Iran. Also, the significant relationship between Malarrash and Oral Ulcer with Anti-Ds DNA's affinity is confirmed by the results of extensive studies on this's affinity, which is also confirmed by the ACR criterion.

Offers

This was the first comprehensive report on the serum level of ANA panel antibodies in Iranian men and women with SLE. For more educational research therapeutic data on SLE, further studies with larger sample sizes are suggested to examine the relationship between ANA Profilling and clinical manifestations.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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