Systemic Lupus Erythematosus among Arabs

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Abstract

Background: The prevalence of clinical manifestations and laboratory parameters in systemic lupus erythematosus differ among various ethnic groups. Few studies have reported on SLE in Arabs.

Objectives: To summarize the demographic, clinical and laboratory features of Arab SLE patients and to compare them with other series from different Arab countries.

Methods: We reviewed the charts of all Arab SLE patients who had been seen at the Carmel Medical Center in Haifa, the Nazareth Hospital and the Holy Family Hospital in Nazareth, and a professional clinic (a referral outpatient clinic of the largest health maintenance organization in Israel) in Acre – all cities in northern Israel. Only patients with symptoms of more than one year were included. Demographic, clinical and laboratory parameters were documented and compared with those of four series from different Arab countries.

Results: The study group comprised 34 patients. The majority of the patients was Moslem; there were a few Druze and one Christian. There was no statistical difference between our patients and any of the other Arab series in terms of arthritis, neuropsychiatric manifestations and VDRL. The presence of serositis and mucocutaneous manifestations was significantly lower in our series compared to some of the other series. However, there was significantly less renal involvement in our patients compared to each of the other series.

Conclusions: The prevalence of most clinical and laboratory parameters in Israeli Arab SLE patients is comparable to that of other series of SLE patients from different Arab countries. The prevalence of renal involvement in Israeli Arab SLE patients seems to be lower than in SLE patients from different Arab countries.

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Systemic lupus erythematosus is a worldwide disease, however the prevalence and severity of the different clinical manifestations differ among ethnic groups [1]. SLE has a higher mortality and greater incidence in black Americans than in white Americans [2,3]. These differences are attributed mainly to differences in genetic and cultural. There are several Arab countries covering a fairly large part of the earth's surface, and Arabs are considered to be a homogenous group of peoples speaking the same language. Few studies have reported on SLE among Arabs [4–7]. In this study we summarize the demographic, clinical and laboratory features of all SLE patients seen in three hospitals and in a referral outpatient clinic in northern Israel.

Patients and Methods

The study group consisted of consecutive Arab patients with the diagnosis of SLE who had been seen in four different settings: Carmel Medical Center (Haifa), Nazareth Hospital and Holy Family Hospital (Nazareth), and a professional clinic (a referral outpatient clinic of the largest health maintenance organization in Israel) in Acre. Only patients with symptoms of at least one year duration, who fulfilled the American College of Rheumatologists criteria for the classification of SLE [8], and whose charts had sufficient clinical laboratory data were included. Patients were usually seen at 1–3 month intervals, and organ involvement was assessed at each visit by clinical and laboratory testing. Kidney involvement was defined as proteinuria > 0.5 g/24 hour urine collection, and active sediment or > 5 red blood cells/high power field in the urine. Leukopenia was defined as leukocyte count of less than 4,000 cells/ml (thrombopenia), platelet count of < 150,000/ml and anemia, and hemoglobin < 11 g/dl.

Antibodies to DNA (Helix Diagnostics, West Sacramento, CA, USA), RNP, Sm, SS-A, SS-B, Scl 70, Jo-1 (Organtec Diagnostics, Germany), anticardiolipin (Corgenix, Westminister, USA), and antinuclear antibodies (Shield Diagnostics, Dundee, UK) were assessed by enzyme-linked immunosorbent assay. Complement (Beckman, Madrid, Spain) and rheumatoid factor (Beckman Coulter, Krefeld, Germany) were assessed by nephelometry, and VDRL by precipitation (Difco, Detroit, USA).

Data on the Arab population in Israel were obtained from the Statistical Abstract of Israel [9]. Categorical variables were analyzed by chi-square and Fisher's exact test.

Results

Forty-four Arab SLE patients were identified. Seven were seen once or twice in the past, but their charts had insufficient clinical and laboratory data. Two patients with symptoms of less than one year duration and one patient with drug-induced lupus (chlorpromazine) were excluded. Of the remaining 34 patients, 18 were from the outpatient clinic in Acre, 3 from the Carmel Medical Center, 6 from the Nazareth Hospital and 7 from the Holy Family Hospital. Demographic data are shown in Table 1. Most of the patients were Moslem (88%), 9% were Druze, and one was Christian. According to the Central

Table 1. Demographic characteristics of the patients

Variable	No. (%)
Female (%)	28 (82)
Family status	
Married (%)	21 (62)
Single (%)	13 (38)
Religious background	
Moslem (%)	30 (88)
Druze (%)	3 (9)
Christian (%)	1 (3)
Family history of SLE	8 (24)
Drugs	
Corticosteroids	34
Anti-malarials	34
Cytoxan	4
Methotrexate	6
Azathioprine	10
Plasmapheresis	1

SLE = systemic lupus erythematosus

Bureau of Statistics in Israel, the percentage of Christians in the Arab population in the areas of our study is about 16%, which is nearly equal to that of the Druze.

Eight patients (24%) had relatives with SLE, including one family in which two sisters and two brothers had the disease. All the patients received corticosteroids for some time, mainly for ongoing musculoskeletal pain and other symptoms or signs that did not respond to other treatments. Many of them are still on a low dose regimen. Four patients were pulsed with high dose corticosteroids, and four patients received cyclophosphamide intravenously for class IV glomerulonephritis (n = 3) and acute cerebritis (n = 1). Antimalarial medication was given to all patients, of whom 28 are currently still taking this medication.

Organ involvement and laboratory parameters are shown in Tables 2 and 3. There was no significant difference in most of the parameters between two or more series, each compared alone to our series. There was no significant difference between our series and any other series in the prevalence of arthritis, neuropsychiatric manifestations and false positive VDRL. On the other hand, there was significantly less renal involvement in our patients compared to any other series. This figure is still significant even after including all 44 patients who were identified. Only seven patients had renal involvement: six had a kidney biopsy showing proliferative glomerulonephritis in five and minimal change disease in one; the seventh patient had mild hematuria that later disappeared. Currently, only one patient has moderate renal failure with hypertension, and three patients have proteinuria 1–2 g/24 hour urine collection. There was no significant correlation between renal involvement and low complement or positive Sm. In contrast, all the patients with renal involvement were Sm negative. Among the patients with neuropsychiatric manifestations (n = 8), five had lupus headache, two had acute confusional state (one of whom also had generalized convulsions), and two had stroke. The latter two patients suffered from antiphospholipid syndrome with recurrent abortions and positive anticardiolipin antibodies, and one of them also had peripheral neuropathy. There was no significant correlation between positive anticardiolipin antibodies or positive Sm and neuropsychiatric manifestations.

Regarding the family with four brothers and sisters having SLE, these patients exhibited different manifestations but all had arthritis and SS-A antibodies. Only one of them (a male) had kidney involvement.

Table 2. Clinical and laboratory variables of our patients compared to those from different Arab countries

Country	Israel	Lebanon	Kuwait	United Arab Emirates	Saudi Arabia
Author (ref)	**Habib and Saliba (present study)**	**Uthman et al. [4]**	**Al-Jarallah et al. [5]**	**Al-Attia [6]**	**Alballa [7]**
Year	**2001**	**1999**	**1998**	**1996**	**1995**
No. of patients	34	100	108	33	87
F:M ratio	4.7:1	6.1:1	9.8:1	15.5:1	8.7:1
Median age at diagnosis (yr)	31	25	31.5	26	28.5 (mean)
Mean duration of disease (yr)	5.1	NA	5.2	4	~5
Clinical features					
Arthritis/arthralgia	94	95	87	91	91
Malar rash	26	52*	43	36	56*
Discoid rash	3	19*	10	3	18*
Photosensitivity	24	16	48*	42	26
Oral sores	15	40*	33*	27	16
Renal involvement	18	50*	37*	54*	63*
Neuropsychiatric	24	19	23	39	26
Serositis	15	40*	29	33	56*
Laboratory features					
Leukopenia	48	17*	83*	30	33
Thrombopenia	12	33*	26	21	20.7
Hemolytic anemia	3	10	NA	9	NA
Antinuclear antibodies	100	87*	94	89.5	98
DNA	85	50*	58*	97	93
Sm	18	NA	13	33	40*
VDRL	12	25	6	9	13

* Significant compared to our series.

Table3. Other clinical and laboratory variables

Clinical variables		Laboratory variables	
Alopecia	29%	Anemia	39%
Vasculopathic skin lesions	12%		
Raynaud's	29%	***SS-A***	***39%***
Fever	15%		
Myositis	3%	***SS-B***	***15%***
Palpable lymphadenopathy	6%		
Pancreatitis	3%	**Low complement**	**52%**
Deep vein thrombosis	6%	Anticardiolipin	45%
Interstitial lung disease	3%	Coombs' test	28%
Recurrent leg abscesses with osteomyelitis	3%	Rheumatoid factor	21%
Ischemic toes	3%		

Discussion

Our series had the lowest female/male ratio compared to the other Arab series. Since the symptoms of SLE appeared in our male patients when they were in their twenties, this ratio could not have an age-related bias. We are unable to explain this finding. The median age at diagnosis is comparable to that in patients from Kuwait but higher than that in other series. The mean duration of symptoms is comparable between the series, giving stronger validity for the comparison between the groups.

Eighty-eight percent of our patients were Moslem. The proportion of Moslems among the Arab population residing in the area covered by our study is about two-thirds, with the rest of the population comprising Druze and Christians; thus we expected 5–6 patients from each of these minorities. Again this could be a referral bias since there are other hospitals in this area. Nonetheless, a difference in the prevalence of some diseases among Arab Moslems compared to Arab Christians in Israel has been reported [10,11].

Eight patients (24%) had relatives with SLE. This number might possibly be skewed by the fact that four members of one family had SLE. Unfortunately, there are no data on familial SLE from other Arab countries. This high familial rate may result from the high prevalence of consanguineous marriages among the Arab population in Israel [12]; in three of the five families with familial SLE the parents of the patients were blood relatives. The question of consanguineous marriages in the Arab population in Israel is of interest since we know that genetic factors play a role in the development of the disease. Yet it is worth noting the different clinical laboratory manifestations exhibited by the family in which two sisters and two brothers have SLE. The parents of this family were not blood relatives. These differences support the importance of environmental factors in the development of clinical laboratory features of the disease. Generally, about 10% of SLE patients have familial SLE. It is more common among first-degree relatives and even more so when the index patient is a male [13].

All our patients received corticosteroids for some time during the course of their disease, mainly for persistent musculoskeletal pain and other symptoms or signs that did not respond to other treatment. Many of these patients are still on a low dose regimen. Azathioprine and methotrexate were given as steroid-sparing agents and methotrexate for those with prominent arthritis. One patient who had ischemic toes was treated with plasmapheresis in addition to other treatments, but eventually the toes became necrotic.

Arthritis/arthralgia was the most common symptom/sign, and this clinical variable was comparable to each of the series. The mucocutaneous manifestations in our patients in general are less prevalent as compared to other series. This difference is significant as compared to two series with regard to malar rash, discoid rash and oral sores, and as compared to one series on photosensitivity. Only one patient in our series had discoid rash, as in the series from the United Arab Emirates. This difference could reflect a true difference or it may be related to the small sample of our patients, or again, to a referral bias where patients with serious skin manifestations are followed at an outpatient clinic in hospitals not included in our study.

Serositis was also less prevalent in our patients. This finding could be related to the fact that echocardiogram and chest X-rays were not performed routinely in our patients. Neuropsychiatric manifestations were comparable to the other series. The two patients who had acute confusional state (including one patient with generalized convulsions and another with memory loss) are doing well without psychiatric or anti-epileptic treatment. The other two patients with antiphospholipid syndrome had no residual motor or sensory deficit and both are receiving warfarin. We could not find a significant correlation between anticardiolipin antibodies and neuropsychiatric manifestations. This lack of correlation could be affected by the small number of our patients.

The major finding in our patients was the significantly low prevalence of renal involvement compared to any other series. This could be a bias due to the fact that most of our patients are seen at a professional outpatient clinic and that patients with serious kidney involvement are followed in hospitals other than those participating in our study. A larger multicenter study would help clarify this issue. At present, only one patient has moderate renal failure. There was no renal mortality or any other death among our patients. There was also no significant correlation between low complement level and renal involvement in our patients.

All our patients had positive antinuclear antibody. The high prevalence could be related to the fact that patients are usually referred to a rheumatologist for evaluation, at least in our referral area, based on positive serology in addition to the symptoms. The routine laboratory workup for musculoskeletal symptoms that is usually ordered by the family physician includes antinuclear antibody, rheumatoid factor, C-reactive protein and antistreptolysin titer.

Our patients had a low prevalence of thrombopenia and hemolytic anemia compared to the other series. The prevalence of anticardiolipin antibodies on our series is relatively high. In most of the patients the anticardiolipin antibody titer was low and some of them had immunoglobulin M antibodies only. Three patients had antiphospholipid syndrome and another two patients had features associated with antiphospholipid syndrome (one with thrombopenia and the other with necrotic toes). There are no data regarding this variable from other Arab series except from the United Arab Emirates (25%). According to the literature the prevalence of anticardiolipin antibodies is 20–50% [14]. Usually a third of them, as in our patients, develop features associated with antiphospholipid syndrome.

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