The characteristics of systemic lupus erythematosus

A study in a general hospital

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ABSTRACT

Objective: There is a wide variation in the natural history of Systemic Lupus Erythematosus among different ethnic and geographical groups. Studies in Arabs are few. This study aims to demonstrate the clinical characteristics of Systemic Lupus Erythematosus patients in Jordanians.

Methods: A retrospective review of the records of the cases diagnosed as Systemic Lupus Erythematosus in a tertiary referral centre (King Hussein Medical Centre) over the years 1991-1997. The records were analyzed for age, sex, presentation, diagnostic criteria, investigations, complications and treatment.

Results: Seventy-six records were analyzed. The patients were from all parts of Jordan, with a mean age of 20 years. The female: male ratio was 24:1. The presentation was arthralgia-arthritis in 68 (89%) patients; skin manifestations in the form of malar rash in 32 (42%), photosensitivity in 19 (25%). Central nervous system manifestations were also noted in 21 (27%) of the patients. Anti-nuclear antibodies were positive in 71 (93%) patients, anti double stranded DNA (DsDNA) positive in 80%. Anemia and leukopenia or both were noted in 52 patients (69%). Erythrocyte Sedimentation Rate was more than 30mm in the first hour in 49 (88%) patients. Lupus anticoagulants were negative in 75% of patients, renal impairment was documented in 46% of the patients (35 patients) with positive correlation to DsDNA. All the patients received steroids, 95% (73) in the form of prednisolone and 5% in the form of methylprednisolone; cytotoxics either cyclophosphamide or azathioprine mainly for renal disease were prescribed to 25 patients, Complications were hypertension (18 patients), renal failure (7 patients), cerebral vascular disease (3 patients). Death was recorded in 3 subjects within 1-4 years of diagnosis

Conclusions: This study demonstrates the presentations of Systemic Lupus Erythematosus patients with a high incidence of complications, which may be due to late presentation or late diagnosis. Further studies are needed on the natural history of this disease in Jordanians.

Keywords: Systemic Lupus Erythematous, complications.

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Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease with a wide spectrum of organ involvement.[1-3] In the recent years there has been a reduction in mortality among patients with SLE in the developed countries. This is resulting from early recognition and treatment of organ affection.[4,5] In developing countries, the disease has been recognized recently, but due to the lack of availability of diagnostic tests, as well as the access to medical care in rural areas make the diagnosis late or missed. Many variations exist regarding the natural history of SLE in different ethnic origins.[6,7]

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Differences between each country could possibly be related to genetic,[8] environmental,[9,10] hormonal,[11] and other influences.[12-16] The studies carried out amongst Arabs are scanty[17-19] with different patterns and characteristics of the groups studied. In Jordan, no figures could be found regarding the natural history of the disease. This study aims to show the spectrum of SLE in Jordanians, with comparison to other Arab and international data.

Methods. The records of all the patients whose final discharge diagnosis was SLE were analyzed. The diagnosis was confirmed by applying the American Rheumatism Association 1982 revised criteria for the diagnosis of SLE.[1] The diagnosis was confirmed if 4 of the criteria were met, irrespective of the time onset of these criteria.

Records. The records were analyzed for the different characteristics of the patients including age, sex, place of residence, and date of diagnosis. The manifestations at presentation and during follow up whether progression of the old manifestations or new manifestations were recorded. Treatment either early or during follow up were also recorded, as well as recording the complications.

Laboratory methods. All the tests were carried out in the laboratory of King Hussein Medical Centre using standardized methods for: Antinuclear Antibodies (ANA), RF, ESR, C4, C3, Coombs test, the extractable nuclear Antibodies (ENA). Due to the cost of some of the tests, they were not performed on all patients, and no criteria could be found on whom these tests were performed; but the more severe the disease the more tests that were requested.

Results. A total of 76 records were analyzed.

Sex. 96% (73 subjects) were females and 4% (3 subjects) were males with a ratio of 24:1.

Age. The mean age of diagnosis was 22.6±1 year (mean±standard error of the mean); with a range of 9-60 years. Table 1 shows the age distribution of the patients.

Date of diagnosis. The date of diagnosis of SLE, ranged from 1969 to 1997. There was a defect in recording the data, or lack of diagnosis from the first recorded case in 1969 to 1980, but afterwards there was a yearly diagnosis of SLE, at a range of 1- 3 cases per year, until 1987 when the rate of diagnosis rose to 6-8 cases per year. Table 2 shows the diagnosed cases per year.

Geographic distribution. The geographical distribution of the cases in Jordan, with Amman area residing 37 cases (49%), Irbid area residing 12 cases (16%), Zarqa area residing 9 cases (12%), while the rest of the governorates had 1.3-5% each.

Manifestations. Arthralgia/arthritis was present in 68 patients (89%) at some time during the natural history of the disease, and also was the presenting feature in most of these cases. Skin manifestations in the form of malar rash were present in 32 patients (42%), photosensitivity in 19 patients (25%), alopecia in 8 patients (10%), and discoid rash in 5 patients (7%); oral ulcers occurred in 13 patients (17%); central nervous system manifestations were present in 21 patients (27%), 12 patients had psychosis while the other 9 patients had seizures; cardiopulmonary manifestations either as pleurisy or pericarditis were present in 20 patients (26%) during the natural history of the disease.

Table 1 - Age distribution among the patients.

Age	Number (Percent of cases)
10-19 years	30 (39)
20-29 years	33 (44)
30-39 years	10 (13)
40-49 years	2 (3)
50-59 years	-
60-69 years	1 (1)

Table 2 - Date of diagnosis.

Year	Subjects
1969	1
1980	1
1982	3
1984	1
1985	1
1986	1
1987	8
1988	3
1989	9
1990	6
1991	6
1992	7
1993	6
1994	8
1995	7
1996	6
1997	2

Laboratory data. Anti-nuclear antibodies (ANA) were positive in 71 patients (93%), anti-double stranded DNA antibodies were positive in 61 patients (80%), hematological manifestations in the form of anemia and leukopenia or both were present in 52 patients (69%), Rheumatoid Factor (RF) was detected in 25 patients (32%); renal involvement in the form of active sediment or proteinuria was noted in 35 subjects (46%). Of all the patients with the disease; other tests were carried out on some patients including coombs test which was performed on 65 patients and was positive in 30 subjects (46% of those tested). Complement components C3 and C4 levels were tested in 57 patients. The level was decreased in 54% and 64%. Lupus erythematosus (LE) cell was performed on 52 patients and was positive in 37 of them (71% of those tested). VDRL test performed on 40 subjects was positive in 12 subjects (16% of the total). Lupus anticoagulants carried out on 32 subjects was positive in 8 subjects (10% of the total), anti-cardiolipin antibody titres carried out on 18 subjects was positive in 9 (12% of the total). Kidney biopsy was performed on 7 subjects, 3 had diffuse proliferative glomerulo-nephritis (GN), 2 mesangial GN, and 2 Focal segmental GN. The Erythrocyte Sedimentation Rate (ESR) used as a screening test, as well as to assess disease was more than 50 mm in the first hour in 68 patients (90%). Anti Sm antibodies were requested in 4 patients, in 2 of them the result was positive, while it was negative in the other 2.

Treatment. All our patients were on steroids; Prednisolone in 74 patients (97%), with methylprednisolone added to achieve remission in 4 patients. Non-steroidal anti-inflammatory drugs (NSAID) were prescribed to 42 patients (52%), Chloroquine to 25 patients (32%), and cytotoxic drugs either azathioprine or cyclophosphamide in 25 patients (32%).

Complications. Complications noted during the natural history of the disease were renal in 33% of cases (25 patients), with renal failure requiring dialysis in 7 and hypertension in the other 18 patients; 8 patients had at least one deep venous thrombosis documented by non-invasive techniques, 3 had pulmonary embolism, 3 cerebrovascular disease, and one had peripheral arterial thrombosis. It was noted that 10 patients had gastrointestinal complications mostly as upper gastrointestinal bleeding, eye complications were noted in 2 patients; there were 4 deaths recorded within 4 years of diagnosis.

Males with SLE. There were only 3 cases of documented SLE in males; all were young with a mean age of 19 years, with a very high ESR, and a positive ANA titers. All had renal involvement, and one is undergoing hemodialysis.

Discussion.

There is a wide difference in the presentation and natural history of SLE between different nations or between different ethnic groups in the same country. This study was carried out on Arabs living in Jordan, with a distribution for all over the country. The figures regarding prevalence of disease are inaccurate due to the lack of national data registry, as well as having a high percentage of undiagnosed cases in the community[20] making the estimation of prevalence unrealistic, but as the Royal Medical Services is responsible for treatment of 50% of population (with many referrals from other public sectors) the estimated prevalence would be 3.4/ 100,000 population.

Comparing our figures to the results from other Arab countries that could be sited on the Medline, there are 2 studies from the United Arab Emirates[16-17] and one study from Saudi Arabia.[18]

The female to male ratio in our study is 24/1, this compares to 27/1 in the United Arab Emirates (UAE), and 9/1 in Saudi patients, which reflects female preponderance, as well as thinking that SLE is rare in males therefore results are under investigation. The diagnosis of SLE started to peak during 1989-1996 with 6-9 cases/per year as compared to 1-3 cases/year before that. This reflects the availability of tests to diagnose SLE due to the large expansion of medical services, and funding of the tests, increased awareness of doctors about this diagnosis, and referral of problem undiagnosed cases to tertiary centers for further evaluation.

The geographic distribution of the cases reflect the population distribution of Jordan, with Amman occupying 50% of the cases. This fact reflects the awareness of the diagnosis in the Amman area, the fact that the complaints may be non-specific, and many females in other governorates will not seek medical advice or seek it late, due to lack of nearby medical facilities or being unable to afford the costs of medical consultation.

Most of our cases (89%) presented with arthralgia /arthritis with the diagnosis confirmed by applying the ARA diagnostic criteria from the history, physical examination and laboratory data. These figures are similar to studies in other Arabs; (91%) UAE, 91% in Saudi Arabia; and also to other studies from different countries. Skin and mucus membrane presentation were malar rash in 42%, (36% in other studies), photosensitivity 25% (42% in other) alopecia 10%, (not recorded in other studies). Discoid rash in 7% (3% in other studies) and oral ulcers in 17% (27% in other studies). Cardio pulmonary presentation, mostly in the form of serositis (pleurisy or pericarditis were noted in 26% of cases. Seizures and psychosis or both did not occur frequently at presentation but were noted in 27% of our patients during follow up as a primary or secondary phenomenon. This is in contrast to studies

from UAE in which no neuropsychiatric complications were noted, but similar to Saudi patients (27%), and in concert with other international data stating the prevalence of 14-75% of patients with SLE depending on the criteria for diagnosis.[21,22]

The laboratory data recorded in our patients were a positive ANA in 93%, positive DsDNA-antibodies in 80%, LE cells in 71% and hematological abnormalities in 69% of the cases either anemia or leukopenia. No other autoantibodies were tested other than 4 patients in whom anti Sm antibodies were tested, mainly due to their high cost and lack of availability, nevertheless, their usefulness in the management of SLE is disputed,[23] and their level may not correlate with disease activity, other than Ds-DNA antibodies.[24] Although Erythrocyte Sedimentation Rate (ESR) has a limited sensitivity and specificity for screening of disease,[25] it was >50mm/hr in 90% of cases, which may indicate the importance of this cheap test as a screening for autoimmune diseases. A varying battery of tests were also performed as Rheumatoid Factor (RF) which was positive in 32%, C4 and C3 was decreased in 54% of cases which may indicate the severity or activity of SLE in our patients, coombs test was positive in 40% of the subjects performed. Lupus anticoagulants performed on 32 subjects were positive in 8 (25%), while anticardiolipin antibodies were performed on 18 subjects, and were positive in 4 (22%). In a meta analysis by Wahl et al[26] the risk of venous thrombosis was 6 times greater for patients with positive lupus anticoagulants, where it was 2 times greater for patients positive for anticardiolipin antibodies; our patients did not show a similar tendency as these tests were negative in patients with venous thrombosis (3 patients), positive in 2 patients with no evidence of thrombosis.

Renal involvement in the form of active sediment, proteinuria and or hematuria occurred in 35 subjects (46%), of which 29 (83%) had a positive DsDNA antibodies, 6 negative, while it was positive in 32 subjects without renal involvement. These findings support the current understanding of pathogenesis of lupus nephritis that is anti Ds-DNA antibodies are neither necessary nor sufficient for nephritis to occur.[27] Comparing our results to nearby countries showed that in a study among Turkish patients with lupus nephritis, most the patients were found to have high levels of Ds-DNA antibodies,[28] while in patients from UAE[17] the level was very high to draw any conclusions. Renal biopsy was performed on 7 subjects of which 4 had diffuse proliferative GN, 2 mesangial and 2 focal segmental GN. Renal complication in the form of hypertension and renal failure or both occurred in 33% of patients.

The treatment options were according to the international recommendation with non-steroidal anti-inflammatory drugs (NSAID) to treat arthralgia used in 52% of cases, chloroquine in 32% of cases but steroids either oral prednisolone in 97% and methylprednisolone or both in 5.2%, combined with cytotoxtic drug therapy (cyclophosphamide or azathioprine) in 32% were predominate treatments. This fact reflects a late presentation, severe systemic involvement, as well as the physicians preference to steroids with rapid onset of response.

The complications noted affected most of the systems with renal involvement first, followed by gastrointestinal complications related to NSAID or steroid intake, vascular presentations or complications noted during the course of SLE were VT in 8 subjects cerbrovascular disease 3 patients pulmonary embolism in 3 subjects abortions in 6 and arterial embolism in one subject. There were 2 patients with complication of the eyes in the form of choroiditis not related directly to drug intake and early cataract most probably related to steroid usage. The recorded mortality among registered patients is 4 subjects and this figure is low owing to poor follow up of the paloutside Amman.

Our male population of SLE is only 3 subjects which is a small number to make any conclusions but all of them had severe symptoms on presentation with renal involvement and positive ANA, all received steroids and one is having renal failure.

This may be due to late presentation, or that the disease is more severe in Jordanian males.

Lastly, as with other retrospective studies, there were limitations related to recording of data, lack of details regarding the treatment courses, lack of recording of the laboratory tests used and proper methodology especially in early records, nevertheless we tried to as comprehensive as possible, to provide an overview of this disease in Jordanians.

In conclusion, SLE is a disease of various presentations and progression. Factors involved in these features are multiple - possibly involving interactions of environmental, genetic factors. Our study in Jordan is similar in certain features to other Arab countries but shows also variations, this may be due to late recognition of the disease or a different natural history of the disease related to environmental factors. Further studies are awaited to answer these questions and many others.

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