October 2000

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Clinical Spectrum of Systemic Lupus Erythematosus at the Aga Khan University Hospital

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Abstract

Background: Systemic lupus erythematosus is a disease of unknown etiology, which at onest may involve only one organ system or he multisystemic. The aim of our study is to determine the clinical presentation of SEE patients presenting to AKUH to establish whether guidelines laid down about this disease are in agreement with our experience.
Methods: A retrospective log review was carried out at AKUH based on data obtained from 165 files of individuals admitted to the hospital over a period of 12 years with a confirmed diagnosis of SLE.
Results: From the sample size of 165, 143 (86.7%) were females and 22 (13.3%) males. The mean age of diagnosis was 30.9 years. Frequency of symptomatology was observed to he in the following order: systemic 78.8%, musculoskeletal 63% and hematological60.6%. On investigation ANA levels were positive in 112 patients.
Conclusion: Our result head us to conclude tI tat the classification set forth b the American Rheumatologic Association is applicable to patients presenting with SEE iii our setting (JPMA 50:364, 2000).

Introduction

Systemic Lupus Erythmatosus (SLE is a disease of unknown etiology in which tissues and cells are damaged by pathogenic autoantibody and immune complexes[1]
The disease is encountered worldwide and can affect any race. It is most commonly found amongst women of childbearing age (female: male 9: 1).The highest frequencies are in Women of Aim—Caribbean, Chinese. Asians and South American Indian ancestry[2].
At onset, systemic. musculoskeletal and coetaneous manifestations are most commonly observed, undue fatigability being cited as the most frequent symptom. The musculoskeletal system is involved in over 90% of the patients with SLE and skin is the target organ in 70% of the cases. Nephritis is still probably the most likely manifestation of S LE to be associated with mortality. I however infection as a result of immunosuppressive therapy is believed to be a Common cause of death in under developed nations. Other manifestations include hematological (85%). neurological (60%), cardio—respiratory (60%), and gastrointestinal (45%)[3].
Tan et.al.[3] in 1982 proposed comprehensive diagnosis criteria for SLE which was based on the initial foundation laid down in 1971 by the American Rheuniatological Association. The study population was broadly representative of the major medical institutions of USA.
Despite the paucity of information concern ing the disease, genetic and environmental factors seem to be the essential contributors towards the development and exacerbation of St .F, For example it is hypothesized that SLE is disease of modernization and therefore its prevalence in a predominately rural population like that of India is low (3.2 per 100000 {95% C.1})[4]. Compared to that in USA (124 per l00000195%C.I)[5]. These factors may influence the clinical presentation of the disease and hence the classification used today may not be entirely' relevant to every individual setting. This concept has been taken up by various research groups such as in Kuwait University[6]. Which describes the clinical characteristics of patients with SLE. This retrospective analysis resulted in bindings. Some of which were similar to those in developed countries and others, which showed differences. These included

hematological and mucocutaneuos manifestations and possibly a low prevalence of anti sm antibodies.
In another hospital based analysis in Malaysia[7], 539 patients with SI ,F. were admitted and hollowed up for a period of 16 years to identify any difference in disease expression between the gender and amongst the 3 major ethnic groups within the country. Results showed that ethnic Chinese were more likely to softer from SLE. whereas Indian patients had the poorest survival rates.
The aim of this study is to determine the clinical presentation of SLE patients presenting to AKUH and to establish whether the criteria defined by Tan et al[3] are in agreement with the local experience. With a few exceptions, there remains a lack of good epidemiological studies in the India subcontinent and hence an analysis of the trend of SLF would be of use in the general body of information available on the subject.

Patient and Method

This study was conducted at the Aga Khan University Hospital (AKUH), a tertiary care medical facility in the city of Karachi. The study design is a retrospective log review of records of SLE patients admitted in AKUII from 1989- 1999. A questionnaire was designed which documented to the spectrum of SLE amongst in-patients admitted at AKUH. Also recorded were features, which may influence the course of the disease, such as family history. age, sex. and place of residence.
The sampling procedure adopted was a convenience sample on which the aforementioned questionnaire was tested. The primary sources of information were the clinical summaries of admission at the time of, or nearest to confirmed diagnosis of SLE. Files in which the diagnosis of SLE was not confirmed. by either serology or skin! renal biopsy, were dropped from the sampling frame. All available histories and reports of investigations carried out during the patients' stay verified this data. A total of 165 files were available for review. The information gathered was entered into Epi info 6.04 and thereby analyzed.

Results

From the sample size of 165, 143 (86.7%) were females and 22 (13.3%) males. The mean age of diagnosis was calculated to be 30.9 years, with the majority of patients falling within 12-40 years of age (54.2%).
Most of the patients (78.8%) presented to AKUH with systemic manifestations, of which the highest frequencies were those of lever (68.5%) and fatigue (43%0. Amongst the commonest presentations were musculoskeletal (63%), cutaneous (6 I .2%) and hematological (60.6%); of which arthralgia (57%), other rashes (36.4%) and anemia (68.9%) were significantly high. The least reported frequencies were those of cardiopulmonary (24.24%) and ocular (3.6%) manifestations.
To assist in establishing complete and comprehensive criteria of clinical spectrum of SLE, the results of investigations carried out in relation to presenting signs and symptoms were also reviewed in our study. Amongst the investigations, notable findings included a mean hemoglobin level of 9.9 g/dI with a 68.9% of the values falling below 11g /dl.
The key investigations used for diagnosis of SLE were serology. Antinuclear antibodies (ANA) levels were positive in all of the 112 patients in whom they were carried out. However, antinuclear double-standard DNA levels were significantly elevated in only 96 patients. Following the diagnosis of SLE, pregnancy was reported in 17 women of which 12 (70.5%) resulted in live births, and 5 (29.4%) resulted in fetal loss. Of all the cases reviewed, 10(16.5%) patients reportedly died.

Table 1. Prominent Clinical Manifestations.

Symptoms	Present		Harrison's*
	no.	%	%
Systemic	**130**	**78.89**	**95**
Fever	113	68.5	95
Fatigue	71	43	95
Malaise	49	29.7	95
Anorexia	45	27.27	95
Weight loss	44	26.7	95
Nausea	40	24.2	95
Musculoskeletal	**104**	**63.05**	**95**
Arthralgia	94	57	95
Myalgia	17	10.3	95
Hand deformity	10	6.1	10
Cutaneous	**101**	**61.2**	**80**
Other rashes	60	36.4	40
Oral ulcers	45	27.3	40
Malar rash	34	20.6	50
Alopecia	32	19.4	40
Photosensitivity	13	7.9	70
Discoid rash	11	6.7	15
Hematological	**100**	**60.6**	**85**
Anemia	102	68.9	70
Leukopenia	27	18.2	65
Thrombocytopenia	34	23.1	15
Lymphadenopathy	23	13.9	20
Splenomegaly	18	10.9	15
Renal	**64**	**38.78**	**50**
Proteinuria	29	23.6	50
Nephrotic syndrome	22	13.3	25
Cellular casts	12	9.8	50
Renal failure	13	7.9	5-10
Gastrointestinal	**61**	**36.96**	**45**
Ascites	13	7.9	<5
Neurological	**54**	**32.7**	**60**
Headache	23	13.9	25
Seizures	18	10.9	20
Psychosis	15	9.1	10
Cognitive dysfunction	13	7.9	20
Peripheral neuropathy	8	4.8	15
Cardiopulmonary	**40**	**24.4**	**60**
Pleural effusion	20	12.1	
Interstital fibrosis	8	4.8	
Myocarditis	6	3.6	
Pleurisy	7	4.2	

*Isselbacher et al., Harrison's principals of internal medicine, 13th ed., 1994, Chapter 11, pp. 1643-48.

Table 2. ANA Pattern (n = 92).

Type	Frequency	%
Homogenous	59	64
Speckled	28	30.4
uclear	1	0.01
Peripheral	3	3
Diffuse	1	0.01

An attempt was made to investigate the association Of the major clinical manifestations of SLL with respect to age and gender. Females were more likely to present with systemic manifestations (84.6% vs40.9%, OR7.94, CI 2.76-23.3 I. p=0M00). No significant differences were seen with cutaneous, renal and rnusculoskeletal manifestations and the frequencies of the presentations of other systems were not high enough to run an)' further tests. There was no significant variation in clinical manifestations found between patients above and below 30 years of age.

Discussion

There is a close agreement between the frequency of positivity of individual variables in our study' population and those quoted in Harrison\'s[1] Females constituted 86.7% of our study' population and this figure is consistent with the predicated value of 90%[3]. Housewives (59.3%, n86) and students (25.8%. n 86) form the bulk of the specified occupation and this was in concordance with the social norms of this region.

Positive family history of autoimmune disorders was elicited in 15 cases. of which 8 were of SLE. As this figure restricts us from probing into the significance of this finding, we are unable to comment on it. However we feel that it may be of use in further studies.

Of the reported comorbids (n=53), hypertension ranked highest (n 26,49.50%), followed by autoimmune disorders (nn9. 16.9%) and the remainder together comprised 44.05%.A possible explanation for the high incidence of hypertension despite the mean age at diagnosis, being. 30 years could he renal involvement.

It night he hypothesized that kidney damage due to the autoimmune process results in hypertension. however the exact mechanism is obscure. Autoimmune disorders tend to present as a complex of two or more disease processes hence accounting for the 16.9% of' the patients who had SLE in conjunction with other autoimmune diseases.

In general, the trends of clinical manifestations of SLE observed in our study. are consistent with the figures quoted in Harrison[1], keeping in mind the American classification set by Tan at al.[3]. The percentages of all variables were lower than in the quoted study, which was excepted, as our study was

only dealing with signs and symptoms at the time of presentation.
Systemic manifestations emerged as the chief presentation in both our study (78.8%) as well as in Harrison's (95%)[1]. Interestingly the Kuwait study[5] calculated the incidence of constitutional symptoms to be 5 1 .4%. In order to enable us to draw a more relevant comparison we referred to "Primer on the Rheumatic Diseases[8] PK, according to which. 53% of patients presented with systemic manifestations, which does not comply with our statistics.
Prominent differences include those in hematological manifestations. Mean hemoglobin level of patients in our study was 9.9 g/dl, with68.9% of patients presenting as anemic (HB: 11 . I g/dl). The Kuwait study[5]. however, reported incidence of hematological manifestations at 53%. A possible explanation for the above findings could be a high prevalence of low hemoglobin levels in females in our population, which could not be distinguished from anemia of chronic disease.
Musculoskeletal involvement emerged as universally prominent with Harrison's[1] classification listing its incidence as 95%. It ranked highest (87%) in the Kuwait study and second (63.5%) only to systemic in ours. Fifty seven percent of patients complained of arthralgia which was the commonest presenting symptom in our study after fever (68.5%).
One hundred one (61.2%) patients displayed mucocutaneous evidence of disease and keeping in concordance with previous studies, the characteristic malar (20.6%) and discoid (6.7%) rash were less frequently reported as compared to other rashes (28.3%).
Fetal loss following diagnosis was 29.4%. However, since the number of pregnancies reported (n I 7) was not high enough for us to be able to draw a significant conclusion, it is worth mentioning here that our figures comply very well with those of the West[1].
During the course of the study a number of limitations were encountered mostly which were related to nature of the study. Being a hospital based study confined to one tertiary care unit; this spectrum could not be generalized to the entire country. Since it was a retrospective log review, information derived from the files of the patients was often incomplete and hence no conclusion could be designed regarding the association of SLE and environment, ethnicity and consanguineous marriage. Access to a considerable number of files was blocked leading to further decrease in sample size.
Hence it can be concluded that the classification set forth by the American rheumatology association in I 984 is applicable to SLE patients in our setting. The files of patients used in our study provided us with information regarding the clinical presentation of SLE, most of which fitted into Tan et al. criteria. It is thus recommended, that doctors continue to use those criteria to assist in diagnosis of SLE.

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