http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i1.62

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

A Clinical, Biochemical and Immunological Profile of Systemic Lupus Erythematosus in Adult Patients in a Tertiary Care Centre

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Abstract
Background: *Systemic Lupus Erythematosus [SLE] is an autoimmune disease. Autoantibodies can be present in many patients for a few years before the 1st clinical symptom appears. Considerable variation has been observed regarding various clinical manifestation of SLE among various ethnic groups as well as various geographical regions. This study was done to elucidate, clinical presenting features and various systemic manifestations, the biochemical parameters, inflammatory markers and immunological profile of the adult SLE in patients presenting to medicine wards of tertiary care centre.*
Methods: *All the adult SLE patients aged 18 years and above attending medicine OPD or admitted in Department of General Medicine during the study period from September 2017 to August 2019were included in the study.*
Results: *In the present study, male:female ratio was 21:1 with most common age group being affected was between 25-44 years. Musculoskeletal system (66.66%) followed by mucocutaneous system (64.44%) were most common systems affected in this study. 23(51.11%) patients had organ threatening lupus affecting kidney and brain. Out of these 23 patients, 43.4% didn't have mucocutaneous or musculoskeletal involvement at all which posed diagnostic challenge. ANA was positive in all patients. Anti dsDNA was commonest autoantibody found in this study. According to SLEDAI, 44.4% patients presented with severe flare.*
Conclusion: *The majority of patients belonged to age group of 25-44 years with a female predilection and ANA was positive in all patients. Out of 23 patients which had major organ involvement at presentation 43.4% didn't have mucocutaneous or musculoskeletal involvement at all.*
Keywords: *SLE, lupus nephritis, neuropsychiatric lupus.*

Introduction

Systemic Lupus Erythematosus [SLE] is an autoimmune disease in which damage to organs and cells initially mediated by tissue binding autoantibodies and immune complexes. Autoantibodies can be present in many patients for a few years before the 1st clinical symptom appears. Susceptibility is same for people of all genders, ages, and ethnic groups.SLE is more common in females as compared to males,

especially in child bearing age group with a ratio ranging from 7:1 to 15:1 due to the role of estrogen in etiopathogenesis of disease. Considerable variation has been observed regarding various clinical manifestation of SLE among various ethnic groups as well as various geographical regions. As SLE is a multisystem disorder affecting all major organs and can be life threatening if it affects kidney and brain. Dermatological or skin manifestation can be very disfiguring. Some patients present only with internal organ manifestations such as nephritis and nervous system manifestations, which poses a diagnostic challenge. This study was done to elucidate, clinical presenting features and various systemic manifestations, the biochemical parameters, inflammatory markers and immunological profile of the adult SLE in patients presenting to medicine wards of tertiary care centre.

Methodology

Total no of 45 adult SLE patients fulfilling SLICC criteria attending OPD or admitted in Dr. D.Y. Patil Medical College and Hospital, Pune during the study period of September 2017 to August 2019 were selected. Institutional ethics committee approval was taken. A written, informed consent was taken from each patient before inclusion.

Inclusion criteria: 45 patients fulfilling the 2012 SLICC classification criteria for SLE coming to medicine OPD and wards, aged ≥18 years.

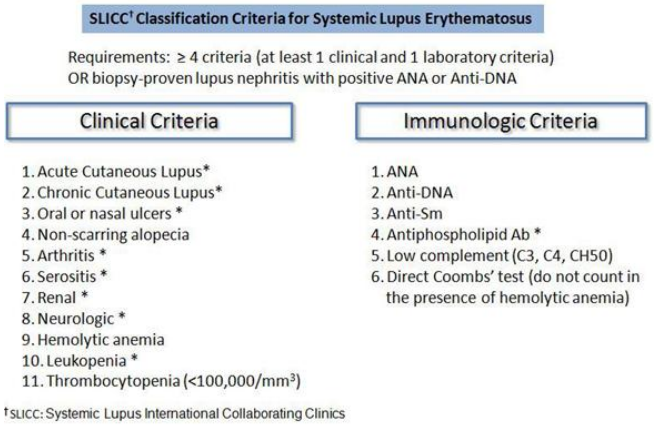


Figure 1: Classification criteria for system lupus Erythematosus.

Exclusion Criteria

- Rheumatoid arthritis and seronegative arthropathy group.
- Other connective tissue disease such as Systemic sclerosis (SSc), Primary Sjogrens syndrome (SS), Mixed connective tissue disease (MCTD), Polymyositis and dermatomyositis (PM/DM) or overlap of SLE and any other disease.
- Vasculitis group.
- Undifferentiated connective tissue disease which does not fulfil criteria of SLE fully (UCTD).

Procedure

A complete history with presenting features were recorded and thorough physical examination was done. Involved joints were counted and evaluated. Number of tender and swollen joints were examined and range of motion seen. Skin and oral features was seen in detail and cutaneous features classified. All systems were examined in detail. Routine investigations such as hemogram, renal function test (RFT), liver function test (LFT), serum protein, urine routine and microscopy, urine protein creatinine ratio (UPCR) and 24 hours Urine protein were done and recorded in all patients. If found anemic, direct Coombs test was done. Inflammatory markers (erythrocyte sedimentation rate and C reactive protein), electrocardiography (ECG), x-ray chest (CXR), ultrasound (USG), and 2 D Echo was done in all patients. Immunological markers such as ANA, ANA blot were done in all patients and reports recorded. ANA was done by either ELISA by Euroimmun ELISA kit or immunofluorescence assay, ANA blot by IMMUNOBLOT method on Euroline test kit. UPCR and 24 hours proteins by colorimetry. If pulmonary involvement was suspected, high resolution computed tomography (HRCT), 6 min walk test and diffusion capacity of carbon monoxide (DLCO) were done to evaluate lung involvement. Renal biopsy was done in indicated patients and findings and grade

recorded. If suspected, antiphospholipid antibody (APLA) and complement levels were done. If required, as in Neurological manifestations, magnetic resonance imaging (MRI) or cerebrospinal fluid (CSF) was done.

Data Analysis: All qualitative and quantitative data was verified and compiled in Microsoft excel and Master chart was prepared.

Statistical Analysis: Data was entered into computer Microsoft Excel and exported to SPSS version 20 for analysis.

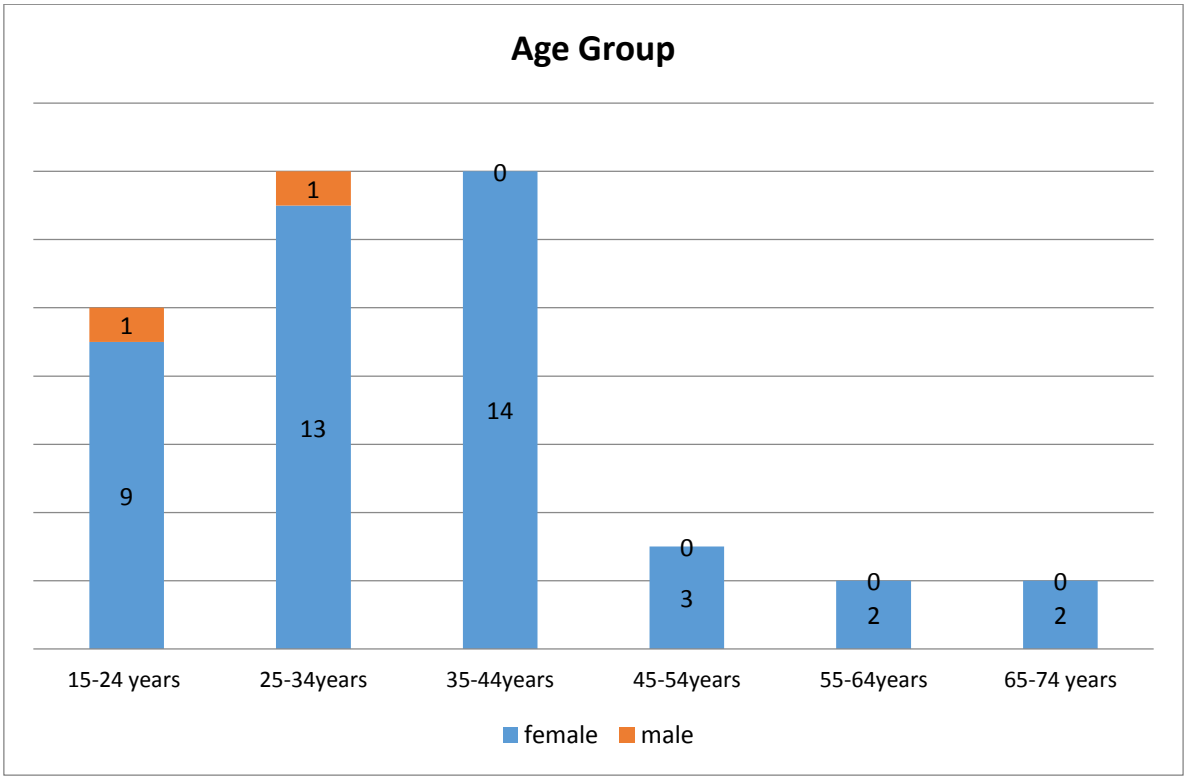
Continuous variables were expressed as mean ± standard deviation or median and range. Categorical variables were expressed as frequency and percentage.

Observations and Results

Table 1: Distribution of SLE patients according to age groups and gender

Age Group	No. of female patients	Percentage of female patients	No. of male patients	Percentage of male patients	Total no of patients	Percentage of total patients
15-24 years	9	20	1	2.22	10	22.22
25-34 years	13	28.88	1	2.22	14	31.11
35-44 years	14	31.11	0	0	14	31.11
45-54 years	3	6.66	0	0	3	6.66
55-64 years	2	4.44	0	0	2	4.44
65-74 years	2	4.44	0	0	2	4.44

This table shows age of patients in this study varied from 18-68 years and most common age group of presentation was between 25-44 years and mean was 33.9 ± 11.5.



Graph 1: Distribution of SLE patients according to age groups and gender

Table 2: Presenting clinical features

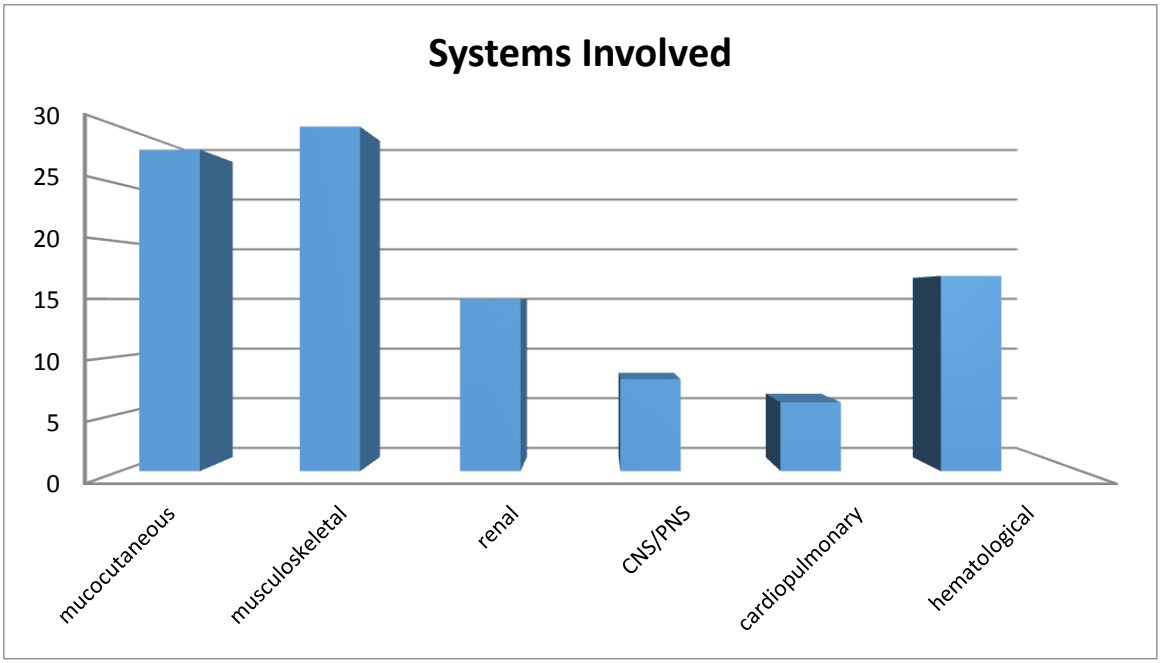
Presenting features	No. of patients	Percentage of patients
Cutaneous Rash	27	60
Oral ulcers	12	26.66
Vasculitic ulcers	3	6.66
Alopecia	14	31.11
Arthritis	30	66.66
Photosensitivity	26	57.77
Fever	7	15.55
Facial puffiness/ pedal oedema	10	22.22
Diarrhea/vomiting/abdominal pain/	5	11.11
Seizures	3	6.66
Headache	1	2.22
Hemiparesis/Quadriparesis	3	6.66
Breathlessness/ palpitations/ chest pain	4	8.88

This table shows arthritis (66.66%) followed by cutaneous rash(60%) was most common presenting feature in this study.

Table 3: Systems involved in SLE

Systems Involved	No. of patients	Percentage of patients
Mucocutaneous	29	64.44
Musculoskeletal	30	66.66
Cardiopulmonary	6	13.33
Renal	15	33.33
Gastrointestinal	0	0
CNS/PNS	8	17.77
Hematological	17	37.77

This table shows musculoskeletal system(66.44%) followed by mucocutaneous system(64.44%) were most common systems involved in this study. 33.33% patients had renal involvement and 17.77% patients had CNS involvement.



Graph 2: Systems involved in SLE

Table 4: Types of skin rash in SLE

Rash		No. of patients	Percentage of patients
ACLE	TEN	1	2.22
	Bullous	2	4.44
	malar	20	44.44
SCLE		1	2.22
DLE		1	2.22
More than one type of rash		2	4.44
Total no of patients		27	60

This table shows among cutaneous rash ACLE was most common type of rash.

Table 5: CNS manifestations in SLE

CNS involvement	No. of patients	Percentage out of total no of patients	Percentage out of total no of neuropsychiatric lupus patients
Seizures	3	6.66	37.5
Stroke	3	6.66	37.5
Cerebral Venous Thrombosis	1	2.22	12.5
Other- mononeuritis multiplex	1	2.22	12.5
Total no of patients	8	17.77	100

This table shows among patients with neuropsychiatric lupus, seizures and stroke were most common presenting features.

Table 6: Urine routine and microscopy findings

Urine analysis		No. of patients	Percentage of patients
RBCs present		15	33.33
WBCs present		9	20
Casts present		0	0
Proteins present		15	33.33
24 hours urine proteins	<0.5 gm/day	30	66.66
	0.5-3.5 gm/day	11	24.44
	>3.5 gm/day	4	8.88

This table shows total 15 patients had proteinuria. Out of these 15 patients, 4 patients presented with nephrotic range of proteinuria.

Table 7: ANA methods

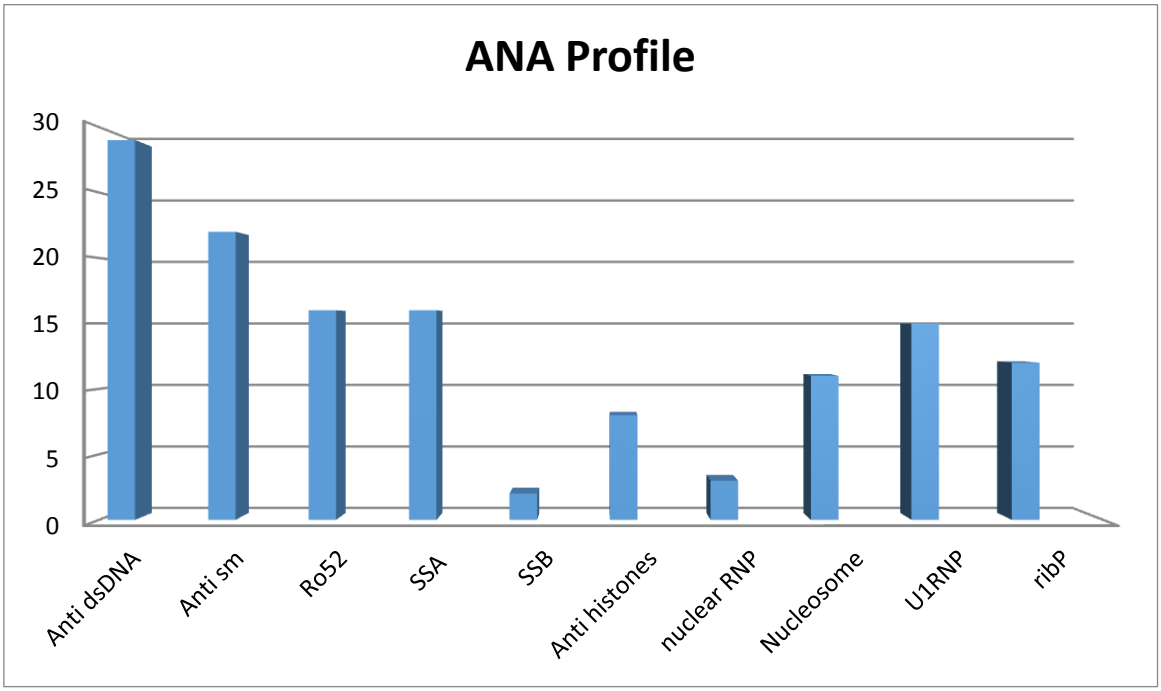
ANA Method			No. of patients	Percentage of patients
ANA by ELISA			38	84.44
ANA by Immunofluorescence	Titers	1+	3	6.66
		2+	2	4.44
		3+	2	4.44
		Total by IF	7	15.55
	Patterns	Homogenous	5	11.11
		Speckled	2	4.44
		Peripheral	0	0
		Nucleolar	0	0
		Centromere	0	0
Total no of ANA positive patients			45	100

This table shows ANA was positive in all 45 patients. ANA by ELISA was done in 38 patients and by immunofluorescence in 7 patients.

Table 8: ANA profile

ANA Profile	No. of patients	Percentage of patients
Anti dsDNA	29	64.44
Anti sm	22	48.88
Ro52	16	35.55
SSA	16	35.55
SSb	2	4.44
Anti-histones	8	17.77
nuclearRNP	3	6.66
Nucleosome	11	24.44
U1RNP	15	33.33
ribP	12	26.66

This table shows Anti dsDNA was most common antibody found to be positive.



Graph 3: ANA profile

Discussion

The present study had total 45 patients out of which, 43 were females and 2 were males. Female to male ratio was 21:1. Binoy et al[1] in India and LUMINA[2] cohort which is multiethnic US cohort suggested, females are affected more likely similar to the present study. Male patients had similar clinical profile as seen in females. Age of patients in this study varied from 18 to 68 years with mean age being 33.9 ± 11.5 years. Highest incidence was found in the age group of 25-34 and 35 -44 years. Binoy et al observed a mean age of disease onset at 21.6 years. The peak incidence rate of SLE in Birmingham, UK was reported between the ages of 18 and 19 years and in the USA was between the ages of 15 and 44 years.[3]

Musculoskeletal system (66.44%) involvement is most common followed by mucocutaneous system (64.66%) in the present study similar to studies done by Malaviya et al[4], Madhavan et al, Mukherjee S et al in other parts of india.87%, 56% and 89.5% patients had musculoskeletal involvement in studies done by Cervera R et[5] al in Europe, Wong K.L. et al,[6] and Al-Attia HM et al[7] in middle east respectively.

Skin manifestation as initial presentation was seen in 29(64.44%) patients.

Most common were malar rash seen in 27(60%) patients and photosensitivity seen in 26(57.77%) patients. TEN, bullous rash, SCLE, DLE type of rash were also seen in 2-4% of patients. oral ulcers (26.66%), vasculitic ulcers(6.66%),

alopecia (31.11%) were common skin manifestations seen in our study. Thus skin manifestations were the second most initial presentation seen in the present study. These findings are similar to studies done in other parts of india as well as in western countries.

Data from studies done in other countries shows higher incidence of renal involvement as initial manifestation compared to the present study. Compared to the present study which had 33.33% patients with renal involvement, Cervera R et al[5], Wong K.L.et al,[6] and Al-Attia HM et al[7]showed 39%, 64.5% and 58% patients with renal involvement respectively. But study done by KC Maloney et al[8] in Jamaica profiled only 16.7% patients with renal involvement which is lesser compared to the present study. Renal biopsy was done on Patients having proteinuria >0.5 grams/day i.e on 15 patients and they were found to be lupus Nephritis on Renal biopsy. Class III followed by class IV lupus nephritis were most common biopsy findings in the present study.

Among 45 patients, 17.77% patients had neuropsyciatric manifestations at the time of presentation. 6.66% patients presented initially as a young stroke and 6.66% patients had seizures at the time of presentation. One patient presented as cerebral venous sinus thrombosis who turned out to be SLE with negative APLA profile. One patient presented as a mononeuritis multiplex without mucocutaneous and musculoskeletal features at the time of presentation is also turned out to be SLE. 27% and 28.5% patients had CNS involvement in studies done by Cervera R et, Al-Attia HM et al respectively at presentation.

Hematological manifestation as initial presentation was seen in 17 that is 37.77% of patients. 17.77% patients presented with leukopenia and 4.44% patients presented initially in form of Idiopathic thrombocytopenia. and 15.55% patients had both leukopenia and thrombocytopenia at the time of presentation. Haemolyticanaemia was seen in 8 to 14%, patients in western countries and in 1 to 7% patients in India but in the present study nobody had haemolyticanaemia. 13.33%patients were having cardiopulmonary system involvement at the time of presentation. 6.66% were having myocarditis, 2.22% had arrhythmia and 4.44% had serositis. Cardiovascular involvement has been reported in 52 to 89% of patients in study by Brigden W et al [9] and by Shearn M. A which is more as compared to the present study.

No patient has gastrointestinal involvement in the present study which was seen in 1 to 2.2% of patients in studies done by Malaviya et al, Madhavan et al.

A.N.A was positive in all 45 patients. ANA positivity was seen 96 and 98% of patients in studies done by Malaviya et al, Madhavan et al, which was 100% in the present study. Anti dsDNA was positive in 64.4% patients in the present study. Anti dsDNA was most common positive antibody seen in studies done by Malaviya et al and Madhavan et al which showed 55% and 65% patients with Anti dsDNA positivity respectively. Studies done in western countries also showed results which are similar to the present study that is ANA positivity in 95-96% of patients with SLE and anti dsDNA is most common positive antibody to be found in SLE patients.

Conclusion

In the present study, male:female ratio was 21:1 with most common age group being affected was between 25-44 years. Musculoskeletal system(66.66%) followed by mucocutaneous system(64.44%) were most common systems affected in this study.23(51.11%) patients had organ threatening lupus affecting kidney and brain. Out of these 23 patients, 43.4% didn't have mucocutaneous or musculoskeletal involvement at all which posed diagnostic challenge. ANA was positive in all patients. Anti dsDNA was commonest autoantibody found in this study.

Abbreviations

SLE- Systemic Lupus Erythematous
ANA- Anti Nuclear Antibody
ACR- American College Of Rheumatology
SLICC- Systemic Lupus International Collaborating Clinics
APLA- Antiphospholipid Antibody
TEN- Toxic Epidermal Necrolysis
ACLE- Acute Cutaneous Lupus Erythematous
SCLE- Subacute Cutaneous Lupus Erythematous
DLE- Discoid Lupus Erythematous

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