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CLINICAL PROFILE AND ITS SEROLOGICAL STUDY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS PRESENTING AT A TERTIARY CARE CENTRE

Medicine

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ABSTRACT

Aim: To determine the clinical & serological profile of systemic lupus erythematosus (SLE) patients at a tertiary care centre in central India. **Methods:** Patients fulfilling the 1982 revised American College of Rheumatology criteria for SLE, seen between December 2018 to May 2020, were included in the study. **Results:** Forty patients of Systemic Lupus Erythematosus were evaluated over a period of one and half year. Arthritis was the commonest initial manifestation followed by fatigue, Photosensitivity and malar rash. Neuro-Psychiatry involvement was present in 52.5% of patients. Among which headache was most common followed by seizures, neuropathy and depression . Cardio-vascular involvement was seen in 17.5% of patients. Pericarditis was most common followed by CAD, Raynaud's phenomenon and pericardial effusion. Pulmonary manifestation was present in 20% of patients in the form of pleural effusion in most of the patients followed by pleurisy, pulmonary haemorrhage and ILD in 2.5% of patients. Gastrointestinal manifestation was present in 32.5% of patients includes nausea, vomiting, dyspepsia. Hepatomegaly was found in 10% and splenomegaly in 11%. Renal manifestation as lupus nephritis was found in 47.5% patients. Proteinuria was most common finding followed by pyuria and haematuria. Under haematological manifestation anaemia was the most common finding seen in 77.5% of patients out of which Normocytic normochromic type was the mos common finding. Significant association of low lymphocyte count with lupus nephritis (P- Value-0.002) and low serum C3 complement level were seen (P-Value-0.023). Low serum C3 complement level was found in 22.5% of patients with mean C3 value of 124.87(mg/dl). There was significant association between low C3 complement level and occurrence of lupus nephritis in SLE patients was found (P- Value -<0.001). Anti-nuclear antibody found positive in all patients. Homogenous immunofluorescence pattern was most commonly seen followed by speckled pattern. Anti-Double stranded DNA antibody was found positive in 62.5% patients. Erythrocyte sedimentation rate was found raised in almost 50% of the patients.

KEYWORDS

Systemic Lupus Erythematosus, Clinical Profile, Arthritis, Haemolytic Anaemia, Tertiary Care Centre.

INTRODUCTION

Systemic lupus erythematous is a chronic autoimmune disease involving multi-organ systems in which production of predominantly non-organ specific auto antibodies are directed towards several self-molecules found in the nucleus, cytoplasm and cell surface resulting in a wide range of clinical manifestations.

Prevalence of SLE in adults is higher as 25-55 per 1 lac in Europe and 160 per 1 lac in United States. Disease onset of SLE patients is between the ages of 15 - 60, 25% present before 16 years, and 20% after the age of 60 years. [1]

Among Asian countries epidemiological information is variable. Prevalence rates usually range within 30-50 per 100,000 populations. This disease typically affects females at far greater rates than males. Women are affected frequently than men nine times more in their reproductive year and then rate declines before puberty and later in life .[2]

SLE is complex disease, as every time the set of symptoms present are not same. This is on account of surrounding factors like the climate, where sunlight plays a role in photosensitivity and skin rashes, or a colder climate can initiate complications such as Raynaud's phenomenon. Symptoms vary widely as SLE is protean in its manifestations and follows a remitting and relapsing course. There is diverse kidney, abnormalities of skin, musculoskeletal haematological, cardiovascular, pulmonary and neurological systems. [1]

In past few year prognosis of SLE has improved remarkably in western countries from 5-year survival rate of 60% in 1960s to a ten-year survival rate of almost 90% in the 1990s.In certain ethnic groups like Caribbean's, Indians and Hispanics a poor prognosis still present.

According to 1982 revised ACR criteria the clinical criteria are Malar rash , Photosensitivity, Nonerosive arthritis, Discoid rash, Oral or nasal ulcers , Serositis, Renal disorder, Hematologic disorder, Neurologic disorder, Positive antinuclear antibody, Immunologic disorder. [3]

Though the clinical profile and serological study encountered in SLE have been well documented in literature, there are very few studies done in India addressing this issue at a tertiary care centre, hence this study is undertaken to check the clinical and serological profile in SLE patients at a tertiary care centre.

MATERIAL AND METHODS

Forty patients satisfying the revised American College of Rheumatology criteria (1982) for SLE were included in the study over a one and half year period. The patients were regularly followed-up, the last follow-up being within 2 months of conclusion of the study.

Clinical assessment included information on medical history, presenting chief complaints, duration of disease, assessment of various organs involvement like cutaneous, musculoskeletal, nervous, cardiopulmonary, and GIT. Routine investigations including complete blood count, ESR, urine analysis, Blood Urea, Serum Creatinine random blood glucose, Thyroid profile, ECG and chest X-ray, 2D echo were done in all patients. Immunological investigations like anti-nuclear antibody (ANA), Complement C3/C4 level, anti-dsDNA were done in all patients, whereas Coombs' test, Rheumatoid factor (RA), USG were done where required.

Inclusion criteria:

1) 40 patients aged over 12 years with a diagnosis of SLE attending Sri Aurobindo Medical College & Postgraduate Institute, Indore. Both in-patients and out-patients were included in the study.
2) Both new and previously diagnosed cases were included in the study.
3) The diagnosis of SLE was made on the basis of the 1982 revised American Rheumatic Association criteria updated 1997; four out of the following criteria were satisfied for diagnosing SLE. [3]

1) Malar rash-Fixed erythema, flat or raised over the malar eminences.
2) Discoid rash-Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur
3) Photosensitivity-Exposure to ultraviolet light causes rash
4) Oral ulcers-Includes oral and nasopharyngeal ulcers observed by physician.
5) Arthritis-Non erosive arthritis involving two or more peripheral joints characterized by tenderness, swelling or effusion.
6) Serositis-Pleuritis or pericarditis documented by ECG, precordial rub or evidence of pericardial effusion.

7) Renal disorder-Proteinuria >0.5 g/dl in 24hr or >3+ or cellular caste.
8) Neurological-Seizures or psychosis without other causes.
9) Haematological-Haemolytic anaemia or disorder
   a. Leukopenia (<4000/µL)or
   b. Lymphopenia (<1500/µL) or
   c. Thrombocytopenia (<100,000 /µL) in the absence of offending drugs
10) Immunological-Anti-ds DNA, anti- smith and / or antiphospholipid antibodies. disorder

- Antinuclear-An abnormal titre of ANA by immunofluorescence or an equivalent antibodiesassay at any point in time in the absence of drugs known to induce ANA

Exclusion criteria:

1. Patients age < 12 years
2. Patients not willing to give written consent or those having malignancies or any other chronic diseases.

RESULTS

Age and sex wise distribution of cases

Forty patients were studied over one and half year period. Among them 37 (92.5%) were females and 3 (7.5%) were male patients. The age of patient was the study ranged from 13-52 year. Mean age in study is 30.3 years. Mean age in female was 30.29 years and in male was 33 years. Most number of patients was in 20-30-year of age group (37.5%).

Musculoskeletal features

The most common presenting complaint was arthritis (65%) in 26 patients followed by fatigue and myalgia (60%) each in 24 patients and next with fever and photosensitivity in 20 (50%) patients each.

Mucocutaneous features

Complaint like hair fall was present in (45%) of patients, menstrual irregularities in (20%) of patients, pedal edema in (30%) of patients, rashes (malar+discoid) in (52%) of patients, alopecia was present in (12.5%) of patients & Oro-nasal ulcer in (32.5%) of patients.

Gastro-Intestinal manifestations:

Finding at the time of diagnosis included hepatomegaly in 4 (10%) and splenomegaly in 6 (11%) of patients.

CNS manifestation

Seizures activity was present in 4 (10%) patients; headache in among different CNS clinical finding headache was most common features present in 11 (25%) patients. Mood disorder and neuropathy were present in 3 patients (7.5%) each.

Cardio-Pulmonary Findings

Pericarditis and pleural effusion were found in 5(12.5%) patients each. Raynaud's phenomenon was present in 3 (7.5%) & pleurisy in 2 (5%) patients.

Table 1- Systemic manifestations

Systemic Abnormalities	Present	Absent	Total
Fever	20 (50)	20 (50)	40
Fatigue	24 (60)	16 (40)	40
Irregular Menses	8 (20)	32 (80)	40
Hair-fall	18 (45)	22 (55)	40
Pedal Oedema	12 (30)	28 (70)	40
Arthritis	26 (65)	14 (35)	40
Myalgia/Arthralgia	24 (60)	16 (40)	40
Oro nasal Ulcer	13	27	40
Malar rash	15	25	40
Alopecia	5	35	40
Photo-sensitivity	20	20	40
Discoid rash	9	31	40
Hepatomegaly	4	36	40
Splenomegaly	6	34	40
Seizures	4	36	40
Headache	11	29	40
Mood Disorder	3	37	40
Neuropathy	3	37	40
Depression	10	30	40
Pleurisy	2	38	40
Effusion	5	35	40
Raynaud's Phenomenon	3	37	40
Pericarditis	5	35	40

Haematological abnormalities

Haematological abnormalities were found in (89%) patients in which includes anemia, lymphopenia, thrombocytopenia, leukopenia, neutropenia.

Table 2- Haematological abnormalities

Haematological Abnormalities	No. of patients	Percentage
Anaemia	30	75.0
Lymphopenia	14	35.0
Leukopenia	04	10.0
Thrombocytopenia	02	5.0

Anemia

It is most common hematological abnormality seen in 31 (77.5%) patients' microcytic type was diagnosed in 8 (20%) patients, anemia of chronic disease (Normocytic) in 21 (52.5%) patients & hemolytic type seen in 2 (5%) of patients. The mean hemoglobin was 10.42 gm% with mean MCV of 82.65%

White blood Cells Abnormalities:

Lymphopenia was most common abnormality seen in 14 (35%) patient with mean lymphocytic count was 24.35% with standard deviation of 9.875%. Lymphopenia was significantly associated with renal involvement.(P value-0.002).Leukopenia was present in 4 (10%) patients with mean value of 5500/mm^3 with standard deviation of 522/mm^3& thrombocytopenia was present in 2 (5%) of patient with mean value of 2.4 lacs.

Renal

Renal involvement was found in 19 (47.5%) patients. Proteinuria was found in 18 (45%) patient and pyuria was in 16 (40%) patients and haematuria in 10 (25%) patients.

Complement level

Low level of C_3 complement was found in 9 (22.5%) patients with mean C_3 level was 124.87(mg/dl) with standard deviation of 44.824. Low c3 complement level was found in 9 patients out of 18 patients having renal involvement and found to be significantly associated with lupus nephritis. [P-value <0.001].

Antinuclear antibodies (ana) and anti double stranded dna antibodies (anti ds- dna)

All the patients were found positive in this study. Homogenous immunofluorescence pattern was seen most commonly in 21 (52.5%) patient followed by speckled 17 (42.5%) and nucleolar 2 (5%). Anti-Ds DNA antibodies were found positive in 25 (62.5%) patients. It is one of the most specific antibodies for SLE.

DISCUSSION

This was an observational study of clinical features of systemic lupus erythematous patients and their laboratory investigations. In our study female preponderance was present as female 37(92.5%) and males 3(7.5%) with a female to male ration of 12.33:1. Similar results were found in an study done by Lisnevskaia L et al, who has reported female to male ratio of 9:1 in a series of adult patient.[4] In an Indian study by Saigal Renu et al described 11:1 female to male ratio. [5]

In our study the mean age of the patients was 30.3 years for male. It is 33 years for female it is 30.29 year. Most of the patients were 20-30-year age group. Ohta A et al noted that most susceptible age for males is 15-44 year and 20-39 years for females. [6].The age distribution described by an Indian study by Aishwarya Sirikonda et al concluded that most of the SLE patients fall in age group of 16 to 48 years with a mean of 26.52 years. [7]

Among 40 patients included in study 26(65%) had initial complaint of joint pain (arthritis) and 24 (605) was complaining of myalgia. These are also most common presenting complaints in our study. Kumar A et al, described frequency of arthritis was 68% and arthralgia was 57% in an Indian study. [8]Among muco-cutaneous manifestation photosensitivity and malar rash are most common finding in our study. Chiewchengchol et al. also stated that malar rash is the most common mucocutaneous skin presentation. [9]In our study fatigue was second most common symptom which was seen in 24(60%) of patients fever in 20(50%) of patients. Batool S et al. documented fatigue in 90% fever in 88% arthritis in 90% of patients. [10]

In our study 40 patient were included among these complaints 4(10%)

patients were presented with seizures. Headache was most common complaints of 11 (27.5%) patients, 10 (25%) were having depression symptoms; neuropathy was occurred in 3(7.5%) patients. In a study of 520 cases by Fatemeh et al, headache was most common neuropsychiatric manifestation in (38.8%) seizures was present in (26.45). [11]

In this study 19(47.5%) was having renal involvement out of 40 patients. Proteinuria was most common urinary abnormality found in 18(45%) patients, micro haematuria in 10(25%) and pyuria in 16(40%) patients. In a study done by John et al, Lupus nephritis was present in 38.3% of SLE patients. [70] In a study by Thomas J.R et al 65% of patients were having albuminuria. [12]

In our study Anorexia, nausea and vomiting are present in almost 50% of patients, which may be due to disease or side effect of drug therapy. In this study among 40 patients 13(32.5%) were having oral ulcers and 4 patients (10%) were having hepatomegaly and 6(11%) were having splenomegaly. This is similar as Sultan M. et al, who described frequency of oral ulcer were 29.2%. [13] Gastritis was seen in 52% cases of SLE patients.

In this study among 40 patients cardio-pulmonary involvement was present in the form of pericarditis in 5(12.5%) patients, coronary artery disease in 2(5%), pleural effusion 5(12.5%) patients seen by 2D-Echo test. Pulmonary haemorrhage was seen in one patient and feature of ILD was seen in one (reticular around glass opacities) patient in HRCT-Chest. Raynaud's phenomenon was seen in 3(7.5%) patients. Ansari Azam et al, described similar results as pericarditis effusion (18%) and pericardial effusion (13%) are most common cardiac manifestation of SLE. [14] In contrast with our result a study by Omer S.B et al, described higher frequency of pulmonary involvement, which is not seen in our study. [15]

In this study anaemia was seen in 31(77.5%) patients, most common was Normocytic normochromic type, in 20% and haemolytic was seen in 2 (5%) of patients. The mean haemoglobin % seen was for 10.42gm%. Similar results were seen in study done by Garcia L et al & Paul BJ et al. [16] [17] Cameron SJ et al previous study documented an association of anaemia with lupus nephritis. However, in this study, there was no such association seen. [18] Similar anaemia results were seen in a study done in India by Sasidharan PK. [19]

In this study lymphopenia was found in 14(35%) patients were the most common WBC abnormality seen. The mean lymphocytic count was 24.35%. Leukopenia was found in 4(10%) of patients & thrombocytopenia in 2(5%) patients. In a similar study leukopenia was found in 84% of cases and was independent of leucopoenia thrombocytopenia was found in 15% of patient. [16] In an Indian study by Sasidharan PK et al documented, thrombocytopenia in 39.8% and leukopenia &lymphopenia in 20%.[19] In our study we have also found significant association of lymphopenia with lupus nephritis and low C_3- complement level. Nesreen Sobhy et al concluded Lymphopenia in 47% patients and those patients have more renal involvement and low complement level. So lymphopenia can be used as a market for renal involvement. [20] Large difference in thrombocytopenia and lymphopenia in difference case studies might be due to large spectrum of disease.

In our study 9 (22.5%) patients have low C_3 complement level with mean C_3 value of 124.87 (mg/dl). In this study we have seen significant association of low C_3 complement with lupus nephritis occurrence. Gandino IJ et al Found higher frequency of lupus nephritis in patients having lower complement levels in SLE.[21] Another study by Sandhu et al also found low complement levels in SLE patients.[22]

In our study, all patients came positive for Anti-Nuclear Antibody which is the most common screening test for SLE patients. Homogenous immunofluorescence pattern was seen mostly in 21(52.5%) followed by speckled 17(42.5%) and nucleolar 2(5%). Anti-Ds DNA was found positive in 25(62.5%) patients. Similar results were found in study done in other region of India. Erythrocyte sedimentation rate were found raised in 52.5% of patients. In our study Anti Nucleosome and Anti Histone Antibody was seen in 5(12.5%) patients.

CONCLUSION

In this study we found female preponderance and mostly it is seen during reproductive age group. Most common presenting complaint was in the form of arthritis, fatigue and myalgia. Among Mucocutaneous manifestation photosensitivity and malar rash were commonly seen. Renal involvement was seen in almost half of the patients and albuminuria was most commonly seen abnormity. There was significant association between lymphophenia and lupus nephritis and low serum C3 complement level were seen. So lymphopenia can be used as a marker for renal involvement in SLE patients. Normocytic normochromic anemia was the most common haematological manifestation. It is important for clinicians to have high index of suspicion for SLE, when patient present with above symptoms as other manifestation of SLE may appear later in course of disease.

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