Original Research Article

FREQUENCY OF DIFFERENT CLINICAL PRESENTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN TERTIARY CARE HOSPITAL

Abstract

BACKGROUND: Systemic lupus erythematosus (SLE) is a multisystem, autoimmune, inflammatory disorder presenting with manifestations from various organ systems.

OBJECTIVE: To determine the frequency of clinical presentations in patients with systemic lupus erythematosus at tertiary care hospital

METHODOLOGY: The cross section study was conducted during 21st October 2018 to 20th April 2019 in the Department of Medicine Civil Hospital Karachi. Total 143 diagnosed patients were included. All patients were evaluated for the initial clinical manifestations including clinical investigations at presentation, Ocular, Mucocutaneous, Pulmonary, Cardiovascular, Gastrointestinal, Musculoskeletal, Hematological, Renal, Neuro Psychiatric, Gynaecological. Descriptive statistics were calculated and stratification was done. Post stratification chi square test was applied. p value≤0.05 was taken as significant.

RESULTS: There were 18.9% male and 81.1% female patient. Mean age was 32.36±9.92 years. Mean SLE duration was 8.16±2.22 months. 79.7% were married and 20.3% were unmarried. In this study among major findings, 52.4% patients were found with fever, 79% with fatigue, 79.7% with arthralgia, 66.4% with weakness, 71.3% with body ache, 35.7% with decreased appetite, 40.6% with headache, 60.1% with photosensitivity, 67.1% with malar rash, 67.1% with alopecia, 60.8% with oral ulcer, 52.4% with raynaud's phenomenon, 52.4% with nausea/vomiting, 33.6% with diarrhea, 31.5% with arthritis, 37.1% with muscle atrophy, 35.7% with osteoporotic fractures, 38.5% with hemolytic anemia.

CONCLUSION: In this study, majority of patients presented with combination of fever, fatigue, arthralgia, weakness, body ache, photosensitivity, and malar rash.

KEYWORDS: Frequency, Clinical Presentations, Systemic Lupus Erythematosus

INTRODUCTION: Systemic lupus erythematosus (SLE) is a multisystem, autoimmune, inflammatory disorder presenting with manifestations from various organ systems.[1,2] Multiple factors including genetic, epigenetic, hormonal, environmental, and immuno-regulatory factors appear to be involved in the expression of the disease.[3] The disease is encountered worldwide and can affect any race. It is most commonly found amongst women of childbearing age.[4] An Indian study showed that prolonged fever was the commonest presenting symptom. Other presenting symptoms with decreased frequency were arthralgia, hemolytic anemia, immune thrombocytopenic purpura, malar rash, generalized tonic clonic seizures, anasarca, splenomegaly, lymphadenopathy, hepatomegaly and goiter.[5,6]UK studies show that in 85% of patients, the first definitive lupus feature was musculoskeletal and/or cutaneous.[5,7] There is a varying epidemiological information regarding SLE among Asian countries. Prevalence rates usually range within 30-50 per 100,000 populations. Incidence rates, vary from 0.9 per 100,000 to 3.1% per annum.[8-9] The etiology and clinical manifestations of SLE, as well as its complications and clinical outcomes, vary among patients.[10] SLE is a complicated disease, as no patient presents with the same set of symptoms.[11] The disease appears to be influenced by ethnic, socioeconomic, and geographical factors.[1,12] There are diverse abnormalities of skin, kidney, hematological, musculoskeletal, pulmonary, cardiovascular and neurological systems.[8, 11] Some studies hypothesize there is a genetic connection between race and lupus which affects disease prevalence. [13, 14] A study reported that 91.40% females and 8.59% males have SLE. The gender

ratio of (female: male) was 10.63:1. Mean age of patients was 33.09±13.34 (15-63). 79.93% were married and 9.04% had family history of SLE. Clinical manifestation showed that 79.03% had fatigue, 78.1% had arthritis, 50.4% had fever, 44.8% had itching, 62% had weakness, 66.8% had body aches, and 57.8% had oedema.[13] In Ocular symptoms; 7.5%, had retinal exudates and blindness, 34.2% had dry eye and 23.5% had conjunctivitis. In Mucocutaneous symptoms; 62.7% had photosensitivity, 73.5% had malar rash, 61.2% had alopecia, 65.2% had mucosal ulcer, 44.9% had raynaud phenomenon[13], 12% had discoid rash[14]. Pulmonary pleuritis was found in 13.9% patients. 35.6% had hypertension, 10.3% had pericarditis and endocarditis symptoms of cardiovascular diseases. 17.19%, 12.97%, 47.8%, 29.1% and 2.4% had splenomegaly, hepatomegaly, nausea/vomting, diarrhoea and melena symptoms of gastrointestinal diseases respectively. In Neuro-Pyschiatric diseases; 30.5% had neuropathies, 53.2% had mood swing, 6.8% had seizures, 11.31% had psychiatric illness and only 2.6% had paralysis. 54.8% had gynecological manifestation.[13] In hematological 25% had leukopenia[12], 6.33% had thrombocytopenia[12.] In renal manifestations, 40.7% had proteinuria[12.] Menorrhagia was found in 25.8%, 24.6 % had amenorrhea and 4.4% had decreased libido.[13] A study reported that 65.6% had neuropsychiatric, 32.8% had cardiopulmonary and 23% had gastrointestinal manifestations.[8] Another study stated that 63% had musculoskeletal, 61.2% had cutaneous, and 3.6% had ocular manifestation.[4]Most of studies have focused on clinical manifestations throughout the course of SLE. Some studies on initial clinical manifestations have been carried out in Pakistan.[15-17] The pattern of presenting clinical manifestations observed in these studies have some similarities. The aim of this study is to delineate the most common clinical pattern and symptoms at onset presentation of Systemic lupus erythematosus patients in the local population.

METHODOLOGY: The cross section study was conducted during 21st October 2018 to 20th April 2019 in the Department of Medicine Civil Hospital Karachi. The calculated sample size was 143 patients using 4% margin of error with the help of WHO software for sample size calculation taking 95% confidence level. The Inclusion criteria were the patients of both genders, patients of age greater than 16 years and less than 50 years and the patient diagnosed with Systemic lupus erythematosus (as per operational definition) for more than 3 months while the exclusion criteria were patients not willing to give written consent, patients with malignancies (was confirmed from clinical history) and those who have drug induced lupus (was confirmed from clinical history).

Systemic Lupus Erythematosus was defined as an autoimmune disease in which the body's immune system mistakenly attacks healthy tissue in many parts of the body. Symptoms vary between people and may be mild to severe. All those diagnosed patients of systemic lupus erythematosus who have anti double stranded DNA antibodies.

The clinical Manifestations include:

Fever: It was defined as body temperature above the normal 98.6 ^{o}F or (37 ^{o}C).

Mucocutaneous manifestations are:

Photosensitivity: It was defined as Rash due to unusual reaction to sunlight.

Malar rash: It was defined as Fixed erythema, flat or raised, sparing the nasolabial folds

Discoid rash: It was defined as Erythematous raised patches with keratotic scarring and follicular plugging

Alopecia: It was defined as the partial or complete loss of hair especially on the scalp either in patches or on the entire head

Raynaud phenomenon: It was defined as Discoloration of fingers and/or toes when a person is exposed to changes in temperature (cold or hot).

Pulmonary manifestations are:

Pleuritis: It was defined as Inflammation of the pleura.

Pleural effusion: It was defined as Accumulation of fluid in pleural cavity.

Cardiovascular manifestations are:

Pericarditis: It was defined as Inflammation of the pericardium.

Hypertension: It was defined as Blood pressure higher than 130 over 80 millimeters of mercury (mmHg).

Endocarditis: It was defined as Inflammation of endocardium.

Ocular manifestations are dry eye, conjunctivitis and blindness.

Conjunctivitis: It was defined as Inflammation of the membrane covering the surface of the eyeball.

Gastrointestinal manifestations are

Splenomegaly: It was defined as abnormal enlargement of the spleen.

Hepatomegaly: It was defined as abnormal enlargement of liver.

Musculoskeletal manifestations are

Arthritis: It was defined as inflammation of joints.

Hematological manifestations are

Anemia: It was defined as Hb <13.5 g/dl in males and Hb <12g/dl in females.

Leukopenia: It was defined as white cell count <4000/mcl

Thrombocytopenia: It was defined as Platelet count < 100,000/mcl

Renal manifestations are

Proteinuria: It was defined as Proteinuria >0.5 g/day or >3+ dipstick proteinuria.

Gynaecological manifestations are

Menorrhagia : It was defined as Heavy menstrual bleeding with blood loss more than 80ml/ period

Amenorrhea: It was defined as Absence of menstruation for 6 months

The patients visited to the department of Medicine and diagnosed with the systemic lupus erythematosus through laboratory test was included in the study. Informed consent from care takers was obtained after an explanation of the study purpose. All patients were evaluated for the initial clinical manifestations of systemic lupus erythematosus (as per operational definition) by the principal investigator including clinical investigations at presentation (i.e. Fatigue, Arthritis, Fever, Itching, Weakness, Body ache, Oedema, Family history), Ocular (i.e. Retinal Exudates, Blindness, Dry eye, Conjunctivitis), Mucocutaneous (i.e. Photosensitivity, Malar rash, Alopecia, Mucosal ulcer, Raynaud phenomenon), Pulmonary (Pleuritis), Cardiovascular (i.e. Hypertension, Pericarditis, Endocarditis), Gastrointestinal (i.e. Splenomegaly, Haepatomegaly, Nausea/vomiting, Diarrhoea, Melena), Musculoskeletal (i.e. Arthritis, Muscle Atrophy, Osteoporotic fracture), Hematological (i.e. Anemia, Hemolytic Anemia, Leucopenia, Thrombocytopenia), Renal (Proteinuria), Neuro Psychiatric (Neuropathies, Mood swing, Seizures, Psychiatric illness, Paralysis), Gynaecological (Menorrhagia and Amenorrhea). The information was collected on a specially designed proforma. Confounders and biasness were controlled by strictly following the inclusion criteria.

Patient's data were compiled and analyzed through statistical package for Social Sciences (SPSS) Version 21. Frequency and percentage were computed for qualitative variables like gender, marital status, clinical manifestations of systemic lupus erythematosus (fatigue, arthritis,

fever, itching, weakness, body aches, oedema, family history of SLE, retinal exudates, blindness, dry eye, conjunctivitis, photosensitivity, malar rash, alopecia, mucosal ulcer, raynaud phenomenon, pleuritis**,** hypertension, pericarditis, endocarditis, splenomegaly, hepatomegaly, nausea/vomiting, diarrhoea melena, neuropathies, mood swing, seizures, psychiatric illness, paralysis, menorrhagia and amenorrhea). Mean±SD were calculated for quantitative variable i.e. age, duration of SLE. The stratification was done on gender, age, marital status, and duration of SLE to see the effect of these modifiers on outcome using Chi-square test. P-value ≤ 0.05 was considered as significant.

RESULTS: Total 143 patients of either gender with age between 17 to 49 years meeting inclusion criteria of study were evaluated to determine the frequency of clinical presentations in patients with systemic lupus erythematosus at tertiary care hospital.

There were 18.9% male and 81.1% female patient. The overall mean age of patients was 32.36±9.92 years. The age was further stratified in two groups. The frequency and percentage of patients among these groups are presented in Graph-1.

The overall mean SLE duration was 8.16±2.22 months. The duration was further stratified in two groups. The frequency and percentage of patients among these groups are presented in Graph-2.

Among 143 patients, 79.7% were married and 20.3% were unmarried. In this study, 52.4% were found with fever, 79% with fatigue, 79.7% with arthralgia, 66.4% with weakness, 71.3% with body ache, 35.7% with decreased appetite, 40.6% with headache and 10.5% with family history of SLE. It was also observed that among total study patients, 60.1% were found with photosensitivity, 67.1% with malar rash, 14% with discoid rash, 67.1% with alopecia, 60.8% with oral ulcer and 52.4% with raynaud's phenomenon. Pleuritis was found for 15.4% and pleural effusion was found for 29.4% patients.

Out of total patients, 12.6% were found with pericarditis, 39.2% with hypertension, 8.4% with endocarditis, 39.9% with dry eye, 23.8% with conjunctivitis and 6.3% with blindness. 11.2% patients were found with splenomegaly, 10.5% with hepatomegaly, 52.4% with nausea/vomiting, 33.6% with diarrhea, 2.8% with melena, 31.5% with arthritis, 37.1% with muscle atrophy, 35.7% with osteoporotic fractures, 28.7% with anemia, 38.5% with hemolytic anemia, 21.7% with leucopenia, 7.7% with thrombocytopenia, 30.1% with proteinuria, 9.1% with seizures, 12.6% with psychosis illness, 32.2 with neuropathies, 50.3% with mood swing, 2.8% with paralysis,

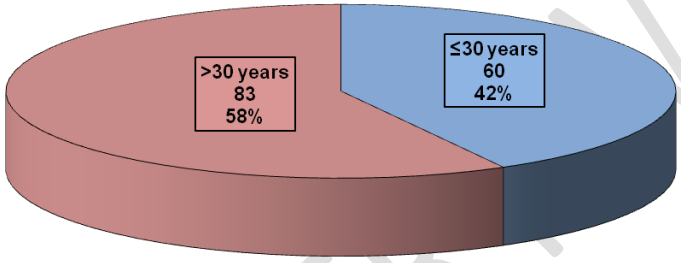
28% with menorrhagia, 30.8% with amenorrhea and 5.6% with decreased libido. The results are presented in Table I-IV.

GRAPH – 1

PERCENTAGE OF PATIENTS

ACCORDING TO AGE GROUPS

(n=143)



GRAPH – 2

PERCENTAGE OF PATIENTS

ACCORDING TO SLE DURATION GROUPS

(n=143)

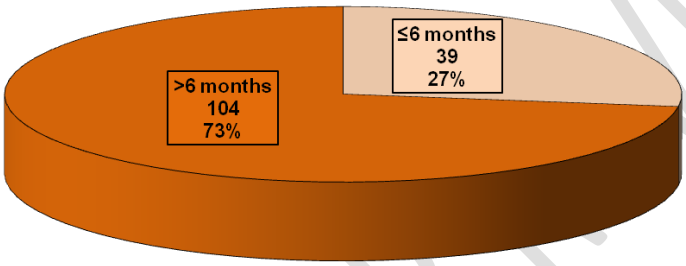


TABLE – I

FREQUENCY DISTRIBUTION OF GENDER

(n=143)

	Frequency (%)
Male	27 (18.9)
Female	116 (81.1)
TOTAL	**143**

TABLE – II

FREQUENCY DISTRIBUTION OF CLINICAL FEATURES

AT PRESENTATION

(n=143)

	Frequency (%)	
	Yes	**No**
Fever	75(52.4)	68(47.6)
Fatigue	113(79)	30(21)
Arthralgia	114(79.7)	29(20.3)
Weakness	95(66.4)	48(33.6)
Body ache	102(71.3)	41(28.7)
Decreased appetite	51(35.7)	92(64.3)
Headache	58(40.6)	85(59.4)
Family history	15(10.5)	128(89.5)

TABLE – III

FREQUENCY DISTRIBUTION OF MUCOCUTANEOUS MANIFESTATIONS

(n=143)

	Frequency (%)	
	Yes	**No**
Photosensitivity	86(60.1)	57(39.9)
Malar Rash	96(67.1)	47(32.9)
Discoid Rash	20(14)	123(86)
Alopecia	96(67.1)	47(32.9)
Oral Ulcer	87(60.8)	56(39.2)
Raynaud Phenomenon	75(52.4)	68(47.6)

TABLE IV: FREQUENCY DISTRIBUTION OF SYSTEMIC FEATURES

CLINICAL FEATURE	FREQUENCY [*n* =143 (%)]	
PULMONARY	**YES**	**NO**
Pleuritis	22(15.4)	121(84.6)
Pleural Effusion	42(29.4)	101(70.6)
CARDIOVASCULAR		
Pericarditis	18(12.6)	87(60.8)
Hypertension	56(39.2)	87(60.8)
Endocarditis	12(8.4)	131(91.6)
OCULAR		
Dry eye	57(39.9)	86(60.1)
Conjunctivitis	34(23.8)	109(76.2)
Blindness	9(6.3)	134(93.7)
GASTROINTESTINAL		
Splenomegaly	16(11.2)	127(88.8)
Hepatomegaly	15(10.5)	128(89.5)
Nausea/vomiting	75(52.4)	68(47.6)
Diarrhoea	48(33.6)	95(66.4)
Melena	4(2.8)	139(97.2)
MUSCULOSKELETAL		
Arthritis	45(31.5)	98(68.5)
Muscle Atrophy	53(37.1)	90(62.9)
Osteoporotic fractures	51(35.7)	92(64.3)
HEMATOLOGICAL		
Anemia	41(28.7)	102(71.3)
Hemolytic Anemia	55(38.5)	88(61.5)
Leucopenia	31(21.7)	112(78.3)
Thrombocytopenia	11(7.7)	132(92.3)
RENAL (PROTEINURIA)		
Proteinuria	43(30.1)	100(69.9)
NEURO PSYCHIATRIC		
Seizures	13(9.1)	130(90.9)
Psychosis illness	18(12.6)	125(87.4)
Neuropathies	46(32.2)	97(67.8)
Mood swing	72(50.3)	71(49.7)
Paralysis	4(2.8)	139(97.2)
GYNAECOLOGICAL		
Menorrhagia	40(28)	103(72)
Amenorrhea	44(30.8)	99(69.2)

DISCUSSION: This study was done to observe the pattern of clinical manifestations of SLE. Few studies on initial clinical manifestations have been carried out in Pakistan.[15-17] The pattern of presenting clinical manifestations observed in these studies have some similarities, however, significant differences were also observed. In a study, mostly patients were young. Mean age at presentation in this study was 26 years, which is comparable with study from central Punjab, and another study from Pakistan reported it to be 31 years.[8,16,17] Females were more in numbers in studies conducted previously.[8,15-17] Similar to Islamabad study, female to male ratio was 4:1, which is in contrast with previous study from Central Punjab, in which it was reported as 16:1.[15,17]

Literature search also showed that female preponderance, it may indicate genetic susceptibility locus on X chromosome.[18] Positive family history of autoimmune disorders was elicited, higher number of indicating familial autoimmunity.[19] The most common complain patients presented with was fatigue. Fatigue is one of the most common, non specific, initial presentation of SLE, reported in literature.[8, 20]

Joint pains ranged from arthralgia to intermittent polyarthritis. Fever was accompanying feature was also reported. Among mucocutaneous manifestations, more than 80% patients had oral ulcers, alopecia, malar rash and photosensitivity. Higher frequency of arthritis in a study in comparison with other study from same region were reported. Few patients had discoid rash.[8]

Renal involvement is common in SLE and is a significant cause of morbidity and mortality. The clinical presentation of lupus nephritis is highly variable, ranging from asymptomatic hematuria and/or proteinuria to frank nephritic syndrome to rapidly progressive glomerulonephritis with loss of renal function.[21] Lupus nephritis, which was mainly glomerulonephritis was present in

75.4% of patients, out of which 24.6% had class IV lupus nephritis, and 18.0% had full-blown nephritic syndrome at presentation in a study.[8]

A variety of gastrointestinal symptoms has been described in literature.[22] Abdominal pain was the most frequent presenting symptom in SLE. Pancreatitis at presentation, having raised serum amylase and lipase along with abdominal pain was reported. Cardiopulmonary involvement as initial presentation of SLE is not frequently reported in literature. 23% had pulmonary manifestations at presentation. Half of these patients presented with pulmonary hypertension, 13.1% had pleural effusion, 6.6% had lung parenchymal involvement and one patient was found to have pulmonary haemorrhage.[8]

In one study, 13.1% had cardiac involvement, half of these patients had valvular diseases at presentation. The frequency of pericardial effusion (18%) was comparable with the other study of Pakistan, however it was higher than that of another Pakistani study. Neuropsychiatric SLE consists of a broad range of neurologic and psychiatric manifestations. The frequency of neurological involvement was higher in a study while in other Pakistani study it was lower.[8]

Among atypical clinical features at presentation, 6.6% patients presented with unilateral deep vein thrombosis and would have impaired fibrinolysis.[23] 4.9% patients had vasculitic infarcts and gangrene. Four (6.6%) had generalized petechial rash at presentation, which was secondary to thrombocytopenia. Anemia was found to be universal finding (98.4%), it matched with previously recorded data, 27.9% had leucopenia and 36.1% had thrombocytopenia on initial presentation. There was no significant difference in haematological findings.[8] Positivity of ANA with indirect immunoflourence testing approaches above 95% using HEP-2 cell line.[24] A study reported positive ANA profile in 90% of patients.[8]

CONCLUSION: In this study, majority of patients presented with combination of fever, fatigue, arthralgia, weakness, body ache, photosensitivity, and malar rash. Almost three-fourth of patients had renal manifestations at initial presentation. Delay in identifying such findings can lead to fatal morbidity and mortality. Therefore, it is important for clinicians to have high index of suspicion for SLE, when patients present with above symptoms, as other manifestation of SLE may appear later in course of disease.

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