ORIGINAL RESEARCH

Clinico-oral Presentation of Systemic Lupus Erythematosus Patients

Malik Adeel Anwar[1], Nadia Naseem[2], Muhammad Arslan Tayyab[3], Saira Elaine Anwer Khan[4], Muhammad Ahmed Saeed[5], Nighat Mir Ahmad[6], Abdul Hanan Nagi[7]

ABSTRACT

Introduction: Systemic Lupus Erythematosus is a multisystem autoimmune connective tissue disease with a wide range of clinical manifestations. Oral ulceration, with other clinical features and laboratory tests, is one of the important component for the diagnosis of Systemic Lupus Erythematosus issued by American College of Rheumatology (ACR).

Material and Method: The study was conducted in Division of Rheumatology, Fatima Memorial Hospital, Lahore, in collaboration with Department of Morbid Anatomy and Histopathology, University of Health Sciences, Lahore. Patients (n=100) qualifying our inclusion criteria were prepared and examined clinically.

Results: A total of 100 patients were included in the study with male: female ratio of 1:9. Mean age was 28.54 ± 10.09, while mean age for disease onset was 23.77± 8.57. Most (51%) of the patients belonged to poor socioeconomic status. On clinical examination, photosensivity was present in 62% patients followed by arthritis (55%) and nephritis (53%). On oral examination, xerostomia (52%), past history of oral ulceration (51%) and oral ulcers present on examination (24%) were seen in Systemic Lupus Erythematous patients. Of all the ulcers found, mostly (42%) were present on the tongue. Moderate xerostomia was the commonest (23%) finding.

Conclusion: Oral lesions are quite prevalent in patients with Systemic Lupus Erythematosus. This study not only highlights the preventive aspects needed to improve the oral health which in turn enhances quality of life as well as compliance to drug therapy in these patients.

Keywords: SLE, Clinical Features of SLE, Oral Features of SLE, Oral ulcers, Xerostomia.

How to cite this article: Malik Adeel Anwar, Nadia Naseem, Muhammad Arslan Tayyab, Saira Elaine Anwer Khan, Muhammad Ahmed Saeed, Nighat Mir Ahmad, Abdul Hanan Nagi. Clinico-oral presentation of systemic lupus erythematosus patients. International Journal of Contemporary Medical Research 2015;2(4):887-891

[1]Postgraduate Student, [2]Assistant Professor, [3]Postgraduate Student, [7]Professor of Pathology, Department of Morbid Anatomy and Histopathology, University of Health Sciences, [4]Senior Registrar, [5]Assistant Professor, [6]Professor of Rheumatology, Division of Rheumatology, Fatima Memorial Hospital College of Medicine and Dentistry, Lahore, Pakistan

Corresponding author: Malik Adeel Anwar, Department of Morbid Anatomy and Histopathology, University of Health Sciences Lahore, Pakistan.

Source of Support: Nil

Conflict of Interest: None

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is the prototypic autoimmune condition affecting multiple organ systems in the body, with a broad field of clinical demonstrations comprising almost all type of tissues and organs. It is an autoimmune disorder, in which the patient's own immune system assaults its own tissues, particularly constituents of the cellular nuclei.[1]

Incidence of Systemic Lupus Erythematosus (SLE) in US population is 20 to 150 cases per 100,000. The prevalence varies among different race.[2] In Asia it accounts for 3.2-19.3 per 100,000.[3] As regard of gender, females are more commonly affected.[4] The ratio between female and male varies from 4.3 to 13.6.[5] Onset of the first attack of SLE before puberty and after menopause is uncommon.[6] Mean age at onset of symptoms was 32 years and mean age at the time of diagnosis of SLE was 34 years.[7]

The pathogenesis of SLE is incompletely understood. It is caused by interaction among various genetic and environmental factors i.e. it is multifactorial disease. It is described by an overall loss of self-tolerance by production of pathogenic autoantibodies by auto reactive B and T lymphocytes resulting in the tissue damage.[8] The foremost contributor of the disease, innate immunity is necessary for the unusual adaptive immune responses in SLE. It is characterized by modification

and regulation of both cellular and humoral immune responses. B cell hyperactivity and genetic aberration leads to the creation of complement fixing of IgG autoantibodies with anti-dsDNA and anti-nucleosome antibodies. Pathological T cell clone that identify double stranded DNA and nucleosome further drives B cell production of DNA autoantibodies.[9] Abnormalities in programmed cell death (apoptosis), immune complex clearance, complement functions and nucleosome processing have been documented to play their role.[10]

Hereditary and genetic susceptibility of the host may predispose to loss of tolerance to self-antigen induced by either exogenous triggers or endogenous metabolic disturbances.[11-12]

The manifestation of SLE may be localized or systemic, depending upon the organ involved. It has been suggested that the range of medical manifestations as well as the reasons of death are different depending on the time of development of the disease. Moreover, it has been hypothesized that SLE tends to enter into diminution in many patients after a long time of progression.[13] The reported prevalence of oral ulcer in SLE is 7–52% of patients. Frequently involved areas in the mouth were buccal mucosa, hard palate, and vermilion border.[14] Studies showed painful mucosal lesions in 57% of the patients. Oral ulcers detected in SLE patients were painless (82%) while discoid lesions were mostly painful. This difference may be due to dissimilarities in the kind of lesion as erythematous lesions are naturally painless.[15] Oral ulcerations are also part of the 11 criteria devised by American College of Rheumatology for the diagnosis of SLE.[16] The objective of the study was to find out the various clinical and oral features with which a SLE patient presents and is present during the treatment. By knowing these clinical features we can device preventive measures to reduce the unwanted sign and symptoms in the patients.

MATERIALS AND METHODS

It was a descriptive study conducted in Division of Rheumatology, Fatima Memorial Hospital, Lahore, in collaboration with Department of Morbid Anatomy and Histopathology, University of Health Sciences, Lahore. The study was completed in 7 months (April-October 2014). A total of n=100 diagnosed patients of SLE of both gender and all age groups were recruited in the current study after getting written informed consent. Patients with any comorbid conditions were excluded from the study. All the patients were examined for clinical and oral changes and data was recorded. The current study was approved by Institutional Review Board of Fatima Memorial Hospital Lahore and Advanced Studies & Research Board of University of Health Sciences Lahore, Pakistan.

STATISTICAL ANALYSIS

Data was analyzed using SPSS version 20. Frequencies and percentages were computed for all categorical variables Mean age and standard deviations were calculated for age of the patients.

RESULTS

Male to female ratio was 1:9. Mean age was 28.54 ± 10.09. Age range of 12-56 years was seen. Mean age of the female patients was 27.93 ± 9.68 years with a range of 12-56 years, while for the males it was 34.67 ± 12.64 years with a range of 17-56 years. The mean age at onset of disease was 23.77± 8.57 with a range of 9-47 years. Mean age at onset of disease for female patients was 23.10 ± 8.21 years with a range of 10-54 years, while for the males it was 30.44 ± 9.69 years with a range of 17-50 years.

A total of 13% patients reported positive family history. Most (51%) of the patients belonged to low socioeconomic status while 39% belonged to middle socioeconomic status with only 10% patients belonging to upper socioeconomic status.

On clinical examination photosensivity was noticed in 62% followed by arthritis (55%) and nephritis (53%) as shown in Table 1. When nephritis was staged, stage II nephritis was the commonest finding as presented in graph 1.

On oral examination, xerostomia was found in 52% patients, past history of oral ulcerations in 51% patients and glossitis in 34% patients as shown in table 2.

Considering the site of oral ulceration during exami-

Clinical Sign and symptoms	Percentage
Photosensivity	62%
Arthritis	55%
Nephritis	53%
Hair loss	23%
Weight loss	16%
Malar Rash	15%
Skin lesions	12%
Psychosis/Seizures	09%

Table-1: Clinical Sign and Symptoms seen in n=100 SLE Patients.

nation, tongue was involved in 10 patients as shown in table 3.

Xerostomia were reported in total 52 patients with moderate xerostomia being the most common (23 patients) finding. Mild xerostomia was found in 12 patients and severe xerostomia was found in 17 patients.

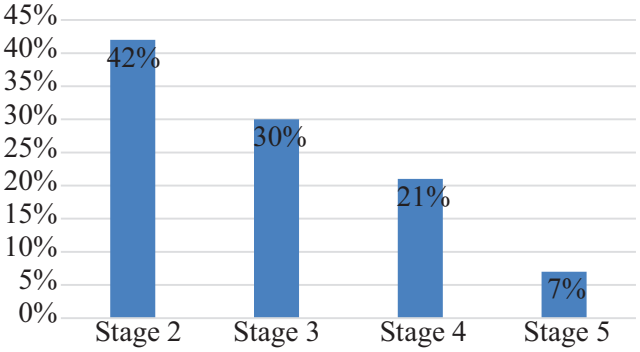
Age, socioeconomic status, skin lesions was strongly associated ($p<0.05$) with duration of disease. Xerostomia was strongly associated with gingival bleeding ($p<0.00$), history of lip lesions ($p=0.028$), arthritis ($p=0.013$). Hair loss was associated with glossitis ($p=0.053$), photosensivity ($p=0.020$) and arthritis ($p=0.011$). Arthritis was also associated with oral ulcerations present on examination ($p=0.024$). No significant association was seen with other studied clinical and oral variables.

Oral Sign and Symptoms	Percentages
Xerostomia	52%
Past history of oral ulcerations	51%
Glossitis	34%
Gingival bleeding	32%
Past history of lip lesions	31%
Painless oral ulcers on examination	24%
Metallic Taste	1%

Table-2: Frequency of oral findings in n=100 SLE Patients

Oral ulcers site	Percentages (Patients out of 24)
Tongue	42% (10patients)
Palate	34% (8 patients)
Buccal Mucosa	21% (5 patients)
Gingiva	3% (1 patient)

Table-3: Frequency of oral ulcers site in n=24 SLE Patients



Graph-1: Different stages of lupus nephritis in n=53 SLE Patients

DISCUSSION

SLE has been a subject of debate comprehensively all over the world. This study is the first from Pakistan reporting the prevalence of oral lesions in association with other clinical variables in patients with SLE. A local study carried out in Karachi, Pakistan, reported mean age of SLE patients being 31 years with an age range of 14-76.[17] In a study from Middle East, the median age of patients with SLE was 26 years while it was 31 years in an American report.[18-19] This data quite concurrent with our findings (Mean Age: 28.54 ± 10 years).

Of n=100 patients (males n=9 and females n=91) male to female ratio in the present study was 1:9 which is strikingly consistent with the studies from Pakistan and US being 1:7.2 and 1:9 respectively.[17,20]

Regarding the socioeconomic status, in the present study, 51% patients belonged to lower and 39% belonged to middle socio-economic status; while 10% patients represented upper class. A study from US. in 2013 also showed that SLE is more common and hits hard in lower socioeconomic class.[21] Similar findings were reported from UK in 1999, where majority of the patients were jobless and from poor background.[22]

Family history in first degree relatives was positive in 13 % of study cases in the present study. No relevant data was found from Pakistan. However a study conducted in Italy showed that 22.7% of SLE patients had a positive family history of auto immune disorder.[23]

Clinical manifestations of SLE found were photosensitivity in 62% patients, followed by arthritis (55%), nephritis (53%), hair loss (23%), malar rash (15%), skin lesions (12%) and psychosis/seizures were observed in 9% patients. A study conducted in Karachi, reported malar rash in 29%, photosensitivity in 6%, and hair-loss in 22%. Arthritis was noted in 38% patients and 14% patients had seizures at some stage during the course of illness.[17] A study conducted in Tunisia reported that 78% patients had articular involvement, 53% had photosensitivity and 63% had malar rash.[24] A study in US found nephritis in 37% of the patients.[21] Skin lesions were reported in a range of 11% to 12.5% in different European studies.[25-26]

As regarding oral changes, gingival bleeding was present in 32% of the patients in the present study. A research from Italy however reported an increase in micro-vascular density to be cause of this bleeding in SLE patients.[27]

On examination, painless oral ulcers were present in 24% of the patients with the commonest site being

tongue (42%). A study conducted by Urman et al in 1978 reported 26% SLE patients presented with oral ulceration with palate being the most commonest site (92%).[28] Xerostomia was found in 52% of the patients in the present study. A study from Norway showed xerostomia in SLE as a major finding in their research.[29] A study from Brazil showed that 58% of SLE patient reported with xerostomia that may be because of IgG deposition in the ductal basement membrane of salivary glands.[30]

CONCLUSION

Females with a positive family history are more prone to SLE so should get a regular checkup. Oral findings predominantly glossitis, gingivitis and oral ulcers are prevalent in patients with SLE that highlights the importance of taking preventive measures to improve the oral health which subsequently will enhance the quality of life as well as compliance to drug therapy of these immunosuppressed patients.

ACKNOWLEDGMENTS

The authors acknowledge the encouragement extended by the Vice-Chancellor of UHS, laboratory staff of Histopathology Department, University of Health Sciences, Lahore and all the staff of Division of Rheumatology, Fatima Memorial Hospital College of Medicine and Dentistry, Lahore for their technical and logistic support.

REFERENCES

1. Bertsias G, Cervera R, and Boumpas DT. EULAR Textbook on Rheumatic Disease. London, BMJ Publishing Group, 2012.
2. Pons-Estel GJ, Alarcón GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. Semin Arthritis Rheum. 2010; 39: 257.
3. Osio-Salido E, Manapat-Reyes H. Epidemiology of systemic lupus erythematosus in Asia. Lupus. 2010;19:1365-73.
4. Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. Medicine (Baltimore). 1993;72:113–24.
5. Petri M. Epidemiology of systemic lupus erythematosus. Best Pract Res Clin Rheumatol. 2002; 16:847-58.
6. Formiga F, Moga I, Pac M, Mitjavila F, Rivera A, Pujol R. Mild presentation of systemic lupus erythematosus in elderly patients assessed by SLEDAI. SLE Disease Activity Index. Lupus. 1999;8:462-5.
7. Font J, Cervera R, Ramos-Casals M, García-Carrasco M, Sents J, Herrero C et al. Clusters of clinical and immunologic features in systemic lupus erythematosus: analysis of 600 patients from a single center. Semin Arthritis Rheum. 2004; 33:217-30.
8. Choi J, Kim ST, Craft J. The pathogenesis of systemic lupus erythematosus—an update. Curr Opin Immunol. 2012;24:651-7.
9. Solangi GA, Zuberi BF, Shaikh SA, Mirza MA. Systemic lupus erythematosus at Karachi and Larkana: A comparative study of 94 patients. JCPSP. 2001;11:371-3.
10. Koutouzov S, Jeronimo AL, Campos H, Amoura Z. Nucleosomes in the pathogenesis of systemic lupus erythematosus. Rheum Dis Clin North Am. 2004; 30:529-558.
11. Liang B, Mamula MJ. Molecular mimicry and the role of B lymphocytes in the processing of autoantigens. Cell Mol Life Sci. 2000; 57(4): 561-8.
12. Kelly JA, Moser KL, Harley JB. The genetics of systemic lupus erythematosus: Putting the pieces together. Genes Immun. 2002; 3: 71-85.
13. Cervera R, Jiménez S, Font J, Ingelmo M. The epidemiology of systemic lupus erythematosus: a review of the current data with special emphasis on the lessons from the Euro-lupus Cohort. APLAR Journal of Rheumatology, 2006;6:150-7.
14. Jonsson R, Heyden G, Westberg NG, Nyberg G. Oral mucosal lesions in systemic lupus erythematosus--a clinical, histopathological and immunopathological study. J Rheumatol. 1984;11: 38-42.
15. Schiodt M. Oral discoid lupus erythematosus. III. A histopathologic study of sixty-six patients. Oral Surg Oral Med Oral Pathol. 1984;57: 281-93.
16. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997; 40: 1725.
17. Rabbani MA, Siddiqui BK, Tahir MH, Ahmad B, Shamim A, Shah SM et al. Systemic lupus erythematosus in Pakistan. Lupus. 2004; 13: 820-5.
18. Haider MA. Clinicolaboratory profile of 33 Arabs with systemic lupus erythematosus. Postgrad Med J. 1996;72:677-9.
19. Pistiner M, Wallace DJ, Nessim S, Metzger AL, Klinenberg JR. Lupus erythematosus in the 1980s: a survey of 570 patients. Semin Arthritis Rheum. 1991; 21:55-64.
20. Weckerle CE, Niewold TB. The unexplained fe-

male predominance of systemic lupus erythematosus: clues from genetic and cytokine studies. Clin Rev Allergy Immunol. 2011;40:42-9.
21. Feldman C, Hiraki LT, Liu J, Fischer MA, Solomon DH, Alarcón GS et al. Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among US adults with Medicaid coverage, 2000-2004. Arthritis Rheum. 2013; 65: 753-63.
22. Sutcliffe N, Clarke AE, Gordon C, Farewell V, Isenberg DA. The association of socio-economic status, race, psychosocial factors and outcome in patients with systemic lupus erythematosus. Rheumatology. 1999;38:1130-7.
23. Priori R, Medda E, Conti F, Cassara EA, Danieli MG, Gerli R et al. Familial autoimmunity as a risk factor for systemic lupus erythematosus and vice versa: a case-control study. Lupus. 2003;12:735-40.
24. Houman MH, Smiti-Khanfir M, Ghorbell B, Miled M. Systemic lupus erythematosus in Tunisia: demographic and clinical analysis of 100 patients. Lupus. 2004;13: 204-11.
25. Rivest C, Lew RA, Welsing PM, Sangha O, Wright EA, Roberts WN et al. Association between clinical factors, socioeconomic status, and organ damage in recent onset systemic lupus erythematosus. J Rheumatol. 2000; 27:680-84.
26. Vilar MJ, Bezerra EL, Sato EI. Skin is the most frequently damaged system in recent-onset systemic lupus erythematosus in a tropical region. Clin Rheumatol. 2005; 24:377-80.
27. Scardina GA, Messina P. Increased gingival blood vessel density in SLE patients. Quintessence Int. 2012; 43:511-15.
28. Urman JD, Lowenstein MB, Abeles M, Weinstein A. Oral mucosal ulceration in systemic lupus erythematosus. Arthritis Rheum. 1978; 21(1): 58-61.
29. Jensen JL, Bergem HO, Gilboe IM, Husby G, Axéll T. Oral and ocular sicca symptoms and findings are prevalent in systemic lupus erythematosus," J Oral Pathol Med. 1999; 28:317-22.
30. Fernandes JD, Nico MM, Aoki V, Bologna S, Romiti R, Levy-Neto M et al. Xerostomia in Sjögren's syndrome and lupus erythematosus: a comparative histological and immunofluorescence study of minor salivary glands alterations. J Cutan Pathol. 2010; 37:432-38.