ORAL ULCERS IN SYSTEMIC LUPUS ERYTHEMATOSUS – RELATIONSHIP WITH DISEASE DURATION AND SEVERITY

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Abstract

Objective: *This study was conducted to assess the prevalence of oral ulceration among systemic lupus erythematosus patients in Pakistan and their relationship with disease duration and severity.*

Materials & Methods: *This cross-sectional study was conducted at Clinic for Arthritis and Rheumatic Diseases, DHQ Hospital, Rawalpindi Medical University, Pakistan. 75 adult patients, fulfilling the 1997 American College of Rheumatology diagnostic criteria for SLE, between January and December 2018 were included in the study. Clinical signs comprising of oral cavity were documented and their relationship to disease duration in years and organ damage using SLICC/ACR-DI score was studied. Descriptive statistics and logistic regression analysis were performed for statistical assessment.*

Results: *75 patients with SLE were included in the study. Female to male ratio was 9.5:1 (94.7% females and 5.3% males) and mean age of patients was 30.65 ± 10.71 years. 34 patients (45.3%) had oral ulcers. No significant association was observed between presence of oral ulcers with age (p-value= 0.43), with gender (p-value= 0.618) and disease duration (p-value=0.10). However, mean SLICC/ACR-DI score for SLE patients with oral ulcers was 2.0 as compared to 0.8 for the patients without oral ulcers (p-value=0.001).*

Conclusion: *This study found that Pakistani patients with SLE have high prevalence (45.3%) of oral ulceration, especially in patients with poorly controlled disease and more evidence of organ damage. This warrants the need to create awareness about disease among healthcare workers and patients.*

Keywords: *Systemic Lupus Erythematosus, oral ulcer, American College of Rheumatology, prevalence, Pakistan*

INTRODUCTION

Systemic lupus erythematosus (SLE) is an auto immune inflammatory disorder of connective tissue with a heterogeneous presentation.[1- 4] It is characterized by formation of various auto antibodies, particularly anti-nuclear antibodies (ANA).[5] Multiple organs get affected such as the heart, brain, kidneys, blood vessels, lungs, skin and muscles.[6] Disease is more prevalent in females, especially at child bearing age.[6,7] A wide range of geographical variations exist in the incidence and prevalence of SLE. Studies have shown that people of Black ethnicity had the highest incidence and prevalence of SLE, followed by Asian and then White ethnic group.[8]

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Several studies have been conducted among Asian population, which reported incidence rates in range of 0.9 to 3.1% whereas prevalence rate was 30 – 50 cases/year per 100,000 population.[9] The prevalence rate of oral lesions specifically reported was 8 – 45%, among which the most common reported manifestation among SLE patients was oral ulcerations.[3,10]

A study conducted on 90 SLE patients in Venezuela, found that 11% patients had oral lesions including white plaque, oral ulceration and erythema.[11] Another research on SLE patients in Saudi Arabia reported presence of oral ulceration among 72% patients.[12]

Limited Data is available on oral features of SLE in Pakistan. The purpose of this study was to assess the prevalence of oral ulceration among systemic lupus erythematosus patients in Pakistan and their relationship with disease duration and severity.

MATERIALS AND METHODS

This prospective, cross-sectional study was carried out at Clinic for Arthritis and Rheumatic Diseases, DHQ Teaching Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan after approval of the study design by institutional Ethics Review Board.

After taking written, informed consent a total of 75 patients (above 16 years of age), fulfilling the diagnostic criteria for SLE as defined by American College of Rheumatology (ACR) 1997, who presented between January 2018 and December 2018 were included in the study.

Exclusion criteria included any co-existent connective tissue disorder (e.g. Rheumatoid arthritis, scleroderma, Sjogren's syndrome, behcet disease), systemic medical illness (e.g. inflammatory bowel disease), dermatological illness and treatment side effects (e.g. methotrexate induced mucositis).

Initial assessment of all patients was done by rheumatologist by taking standard medical history and physical examination. Symptoms and clinical signs comprising of oral cavity, were documented. Consultation from dentist was sought only if clinically warranted.

Registered data included demographic profile (such as age, gender, date of visit), clinical data (presenting features, ACR diagnostic criteria fulfilled and auto-antibody profile at the time of diagnosis, disease duration, treatment taken including methotrexate, clinical signs comprising of oral cavity and disease activity).

Organ damage was determined for each patient according to SLICC/ACR-DI.

Descriptive statistics and logistic regression analysis were performed for statistical assessment. All descriptive statistics are presented as means and standard deviations (SD) for quantitative variables, and as relative frequencies and percentages for categorical variables. Relationship of presence of oral ulcers to disease duration in years and organ damage using SLICC/ACR-DI was studied by logistic regression. ODDS ratio and 95% confidence interval were used to present the strength of association. Level of significance was taken as ≤ 0.05.

All data was collected on pre-designed forms, and then entered into Statistical Package for the Social Sciences (SPSS) version 18 for analysis.

RESULTS

Demographic Characteristics: A total of 75 Pakistani patients with adult onset SLE met the inclusion criteria and were included in the study. Female to male ratio was 9.5:1 (94.7% females and 5.3% males). Mean age of the patients was 30.65 ± 10.71 years. Average duration of disease at the time of enrollment in study was 3.89 years.

Prevalence of Oral Ulcers: SLE patients presenting with oral ulcers were 34 in number (45.3%). No association of age with presence of oral ulcers was observed as the difference in age between SLE patients presenting with and without oral ulcers was statistically insignificant (p-value= 0.43). 2 out of 4 (50%) male patients and 32 out of 71 (45.1%) female patients presented with oral ulcers. No significant association was observed between gender and presence of oral ulcers (p-value= 0.618).52.9% patients (18 out of 34 patients) with oral ulcers had disease duration of less than 2 years while 47% patients (16 out of 34 patients) with oral ulcers had disease duration of more than 2 years (p-value=0.10)

Organ Damage: The mean SLICC/ACR-DI score for SLE patients with oral ulcers was 2.0 as compared to 0.8 for the patients without oral ulcers (p-value=0.001)

1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus

Criterion	Definition
Malar Rash	Fixed erythema, flat or raised, over the malar eminences, trending to spare the nasolabial folds
Discord rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
No erosive Arthritis	Involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion
Pleuritis or Pericarditis	Pleuristis-convincing history of pleuritic pain or rubbing heard by a physician or evidence of pleural effusion OR
	Pericarditis-documented by electrocardiogram or rub or evidence of pericardial effusion
Renal Disorder	Persistent proteinuria > 0.5 grams per day or > than 3+ if quantitation not performed
Neurologic Disorder	Seizures-in the absence of offending drugs or known metabolic derangements e.g., uremia, ketoacidosis, or electrolyte imbalance OR
	Psychosis-in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance
Hematologic Disorder	Hemolytic anemia-with reticulo-cytosis OR
	Leukopenia--< 4,000/mm2 on ≥ 2 occasions OR
	Lymphopenia--< 1,500/mm2 on ≥ 2 occasions
Immunologic Disorder	Anti DNA: Antibody to native DNA in Abnormal titer OR
	Anti-Sm: presence of antibody to Sm nuclear antigen OR
	Positive finding of antiphospholipid antibodies on:
	An abnormal serum level of IgG or IgM anti cardiolipin antibodies,
	A positive test result for lupus anticoagulant using a standard method or
	A false-positive test result for at least 6 months confirmed by treponema pallidum immobilization or fluorescent treponemal antibody absorption test
Positive Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs

DISCUSSION

This present research was conducted to study the existence of oral ulceration among patients with systemic lupus erythematosus in Pakistan. A total of 75 patients who fulfilled the 1997 American College of Rheumatology (ACR) criteria for SLE were included. Our sample's mean age was 30.65 ±10.7. A study conducted in Qatar on 77 patients found mean age of 38.3 ±10.6 years,[13] while another study in Saudi Arabia on 624 patients found the mean age of SLE patients to be 34.3 ±11.9 years.[14] A study in South Tunisian on 146 patients found the mean age of 29.2 years (range 6-55).[15]

A study done in Pakistan found the mean age of 25.97 years in SLE patients[16] Whereas another study done Pakistan is consistent with our study where the mean age of their study was 31 years.[17] Pakistan has relatively younger lupus patients as compared to other populations.

The female to male ratio in current study was 9.5:1. This was exactly similar to the study done in Qatar where they ratio was 9.5:1.[18] A similar ratio was reported in Saudi Arabia 9.8:1,[19] in China 9.6:1.[20] Lower ratios were found in Iran 6.5:1.[21] and in Spain 8:1[22] A study done in Pakistan 9:1.[16] These ratios confirm the female predominance of this disease.

In our study, a high percentage (45.3%) of oral ulceration was observed among SLE patients, which is comparable to study done by Moc[23] in Hong Kong where he found 55% of oral ulceration in SLE patients and Durcan[24] who found oral ulceration among 51% of the SLE patients. In a local study, the incidence of oral ulceration was seen only in 24% of the patients.[16] and another local study by Rabbani et al found it to be 20%. The frequency of oral ulceration may be higher than the other local

studies because of the demographic location, lack of health awareness or lack of approach for female patients to the tertiary care centers. Furthermore, differences in severity of SLE have been observed to be related to different genotype.[23] As many genes have been identified, lupus may also have a different genetic cause in Pakistan

That is responsible for varying susceptibility and expression of disease. Oral ulcers were observed more frequently in patients with high disease activity and more evidence of organ damage, irrespective of disease duration. This warrants the need to create awareness among healthcare workers regarding early diagnosis, regular follow up and better control of disease.

Our study, involved some limitations that should be considered. We studied prevalence of oral ulceration in a referral clinic population who have a relatively higher disease activity as compared to SLE patients under care of primary care physicians. It would be interesting to study the relationship of auto-antibodies to oral lesions, which could not be done in our study due to financial constraints. Socioeconomic factors and the fact that Pakistanis are not familiar with this pathology probably influenced the size of the studied population.

Larger multi-center studies are needed to better understand the characteristics of SLE patients in Pakistan. Epidemiological studies on SLE prevalence, incidence, environmental influence, ethnicity and genetic factors are also warranted as there are no national epidemiological data for this disease.

CONCLUSION

This study found that Pakistani patients with SLE have high prevalence (45.3%) of oral ulceration, especially in patients with poorly controlled disease and more evidence of organ damage. This warrants the need to create awareness among healthcare workers regarding early diagnosis, regular follow up and better control of disease.

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DISCLOSURE STATEMENT

The authors have declared no conflicts of interest.

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