Oral manifestations, oral health status and saliva composition changes in a sample of Iraqi systemic lupus erythematosus patients

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease associated with significant morbidity and mortality. Sicca symptoms are frequent in SLE which may be related to concomitant occurrence of Sjögren's syndrome (SS). The aims of study were to determine prevalence of oral manifestations and tempromandibular joint disorders, and to find a correlation between the changes in saliva flow rate, pH and composition with the incidence of dental caries in SLE patients.

Subjects, materials and methods: One hundred and two individuals were enrolled in this study; 52 of them were SLE patients; and 50 were healthy control individuals matched in age and gender. The assessment of dental status was made according to the decay missing filling teeth (DMFT) index; the gingival inflammation was assessed using the criteria of gingival index; Clinical pocket depth was measured with periodontal probe type William, and whole unstimulated saliva samples have been collected from each subject for biochemical analysis. Also, salivary flow rate and pH were measured. After centrifugation, the supernatant of saliva was aspirated for biochemical analysis.

Results: Oral ulceration was the most prominent orofacial manifestations of SLE patients followed by Tempromandibular joint (TMJ) disorders and facial skin rash then oral vesicles& bullae, oral lichen planus and finally oral petechiae & purpura. Salivary flow rate and salivary pH were significantly lower in SLE patients than in the control subjects. Oral hygiene index (DMFT index, gingival index, Clinical pocket depth) were significantly higher in SLE patients than in the control subjects .Salivary calcium, sodium, chloride, and total protein were significantly higher among SLE patients than in the control subjects. While salivary potassium and inorganic phosphorus were significantly lower among SLE patients than in the control subjects. In addition, there was a highly significant positive linear correlation between age of SLE patients and DMFT, and between age and clinical pocket depth; and a highly significant negative linear correlation between salivary flow rate and salivary calcium in SLE patients. Also there was highly significant positive linear correlation between DMFT and salivary calcium, and between DMFT and salivary chloride.

Conclusions: Oral manifestations are common in Iraqi SLE patients. Changes in salivary flow rate, pH, salivary composition, and increased dental caries may serve as potential markers of the extent of autoimmune mediated salivary gland dysfunction which is similar to Sjogren's syndrome.

Keywords: systemic lupus erythematosus, Oral manifestations, saliva. (J Bagh Coll Dentistry 2012; 24(Sp. Issue 2):65-69).

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a clinical heterogeneous disease which is autoimmune in origin, and characterized by the presence of auto antibodies directed against nuclear antigens. It is by definition, a multi-system disease and patients can present in vastly different ways [1].

The clinical heterogeneity of this disease is mirrored by its complex aetiopathogenesis reviewed [2].

Dysfunction in immune regulation plays the principal role in the pathogenesis of SLE. Hyper reactivity of B-cells, producing a spectrum of autoantibodies, is primarily responsive for the immune dysregulation, although T-cells are involved in the pathogenesis as well. The tissue injury is caused by immune complexes, deposition of which induces cell infiltration and damage to the tissue by proteolytic and collagenolytic enzymes [3].

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The American College of Rheumatology established eleven criteria in 1982 and revised in 1997 [4] as a classificatory instrument to operationalise the definition of SLE in clinical trials.

Oral manifestations like recurrent infections or mouth ulcers, severe gingivitis, or excessive dental caries have been found frequently in SLE [5]. Many patients with SLE suffer from tempromandibular joint disorders, which are a painful complication of the mandible joint that can impair the ability to speak and chew; Osteonecrosis of the mandible frequently leads to articular collapse, bone destruction and loss of function with varying clinical mandibular dysfunction. This manifestation can also be associated with poor oral hygiene, increasing the risk of oral infections and tooth extraction [6].

SLE is closely associated with excretory gland involvement. Thus, oral and ocular symptoms are frequent findings. Minor salivary gland lymphocytic infiltrates are found in 50-75% of the patients; whether they are complaining of dry mouth or not [7].

Unstimulated salivary flow rate is decreased in many of the SLE patients; also SLE is a diagnostic component of secondary Sjogren's syndrome (sSS) [8].

MATERIALS AND METHODS

This study was carried out during the period from the middle of November 2010 till the end of March 2011 in Baghdad city The total sample examined in this study consisted of 102 subjects; they were divided into 2 groups; 52 patients (SLE group); 50 patients were females (96.1%) and two patients were males (3.8%); 50 healthy control females (healthy control group). Informed patients consent and ethical approval were obtained for this study; all patients were diagnosed by a Rheumatologist as SLE patients depending on the criteria of the ACR, 1982. All the subjects answered a written questionnaire regarding their name, age, gender, occupation, dental and medical histories, feeling of dry mouth, any oral, and systemic diseases, SLE duration, SLE activity using SLE disease activity index (SLEDAI) [9] and drugs used in the management of the disease, further complications associated with SLE and all investigations (hematological and immunological) were recorded. Examination of the tempromandibular joint was done and all clinically evident changes (clicking, limitation, dislocation…etc) was determined and recorded. Intraoral examination was done for each individual [10] All clinically evidences of mucosal alteration (redness, swelling, ulcer, etc.) was determined and recorded, to find any oral manifestations. The assessment of dental status was made according to the (Decayed, Missed, and Filled Teeth index); the gingival inflammation was assessed using the criteria of gingival index; clinical pocket depth was measured with periodontal probe type William; whole unstimulated saliva samples have been collected from each subject for biochemical analysis. Salivary samples were collected by spitting method. Saliva pH was measured immediately by digital pH meter; salivary flow rate was measured by collection of saliva through 10 minutes, the volume of saliva is recorded in order to give the salivary flow rate in ml/min; after centrifugation the supernatant of saliva was aspirated for biochemical analysis. Calcium, sodium and potassium were measured by using Atomic absorption spectrophotometer; while inorganic phosphorus, chloride and total protein were measured by colorimetric method. Oral manifestations, saliva flow rate, pH, oral health indices, salivary (Calcium Sodium and Potassium Inorganic phosphorus, Chloride and Total protein) of SLE patients were recorded according to (age, duration of disease, disease activity, and treatment) subgroups.

RESULTS

The mean age of SLE patients was 32.24± 9.26 years, with age range of 16-53 years old, while the mean age of healthy control subjects was 29.24± 7.87years, and range of 17-54 years old, according to the age, SLE patients were divided into four sub-groups (15-24, 25-34, 35-44, 45-54) years. It has been shown that the highest percentage of SLE patients and control subjects was in the age group of 25-34 years. Patients with SLE have been divided into four sub-groups according to disease duration periods (< 1, 1-4, 5-9, 10-14) years; it has been shown that the number of SLE patients of (1-4 years) duration period was significantly higher (P< 0.01).SLE patients have been divided according to treatment into three sub-groups: patients on corticosteroid therapy (Predinisolone) (34%), patients on antimalarial drugs (Hydroxychloroquine) (26%) and patients under combination of medications which include: Predinisolone, Hydroxychloroquine and Immunosuppressive drugs (Azathioprine) (40%) with no significant differences in the percentage of SLE patients according to their treatment.

It has been shown that the number of systemic lupus erythematosus patients with active disease in this study was significantly higher than the number of systemic lupus erythematosus patients with inactive (remission) disease according to SLEDAI.

Table 1: Orofacial manifestations in SLE patients

Orofacial manifestations	N	%
Oral ulceration	36	72
Lichen planus	4	8
TMJ Disorders	27	54
Facial skin rash	27	54
Petechiae and purpura	2	4
Vesicles and Bullai	5	10

Oral ulceration (72%) was the most prominent orofacial manifestations of SLE patients followed by tempromandibular joint (TMJ) disorders (54%) and facial skin rash (54%) then oral vesicles& bullae (10%), oral lichen planus (8%)and finally oral petechiae & purpura (4%). Salivary flow rate and salivary pH were significantly lower in SLE patients than in the control subjects (0.36±0.21 versus 0.85±0.29 ml/min, p <0.001; 6.34±0.60 versus 6.74 ± 0.51, p=0.001 respectively).Oral hygiene index (DMFT index, gingival index, Clinical pocket depth) were significantly higher in

SLE patients than in the control subjects (p <0.001).

Table 2: The mean values of different salivary elements in both SLE patients and control subjects:

Salivary elements	SLE (N=50)		Control (N=50)		t	P
	Mean	SD	Mean	SD		
Calcium (µmol/L)	2.35	0.26	1.60	0.23	15.112	0.000
Potassium (µmol/L)	7.77	1.38	21.58	6.68	-14.318	0.000
Sodium (µmol/L)	10.60	2.54	8.76	2.06	3.985	0.000
Chloride (µmol/L)	40.23	5.86	36.36	4.76	3.626	0.000
Inorganic Phosphorus (µmol/L)	4.47	0.85	7.15	1.74	-9.747	0.000
Total Protein (g/100ml)	0.21	0.06	0.13	0.03	7.249	0.000

Significant using t-test, p <0.001

Salivary calcium, sodium, chloride, and total protein were significantly higher among SLE patients than in the control subjects (P<0.001).While salivary potassium and inorganic phosphorus were significantly lower among SLE patients than in the control subjects (P<0.001).In addition, there was …a highly significant positive linear correlation between age of SLE patients and DMFT(r=0.434,p= 0.002**)**, and between age and clinical pocket depth (r=0.355, p=0.012**)**; and a highly significant negative linear correlation between salivary flow rate and salivary calcium in SLE patients(r= -0.396, p=0.004). Also there was highly significant positive linear correlation between DMFT and salivary calcium(r=0.323, p=0.022**),** and between DMFT and salivary chloride (r=0.325, p=0.021**)**.

DISCUSSION

In the present study 50 SLE patients were females; only 2 patients were males and were statistically excluded. The female to male ratio was 25:1, this was agree with other studies who found that the number of SLE female patients was higher than SLE male patients [11,12,13], found that the female to male ratio was 27:1,37:2 and 17:1 respectively. Oral ulceration was the important oral manifestation of SLE patients in the present study which was present in 72% of those patients. Oral ulceration is commonly found in patients with SLE and represents one of the 1982 revised ACR criteria for the classification of SLE. Oral ulcers are present in roughly 25% to 45% of SLE patients. Oral ulcerations in SLE patients have for a long time been considered as a sign of "vasculitis" and predictors of severe systemic flares of the disease [14]. In the present study 8% of SLE patients were with oral lichen planus which agreed with other study [15] who found that Classic lesions of lichen planus (LP) was uncommon and the chances of conversion of the syndrome into systemic lupus erythematosus are 5-10%.

Facial malar rash was found in 54% of SLE patients in the present study, this agrees with other study [16] who found that 58% of SLE patients have malar rash. Tempromandibulare joint disorders were found in 54% of SLE patients in the present study, other study documented the prevalence of TMJ disorders was 60% in SLE patients [17]. Autoimmune disorders, such as rheumatoid arthritis and lupus erythematosus can cause significant inflammation and destruction within the TMJ, Joint disease associated with lupus, is associated with high concentrations of inflammatory mediators within the joint but sometimes is triggered by system-wide immune dysregulation; Pathophysiology of autoimmune-based arthritis of the TMJ is the same as that found in other joints [18].

In the present study oral petechiae and purpura found in 4% of SLE patients, Thrombotic thrombocytopenic purpura (TTP) in patients with SLE is extremely rare. The overall incidence of TTP in SLE patients is unclear and has been reported to be as low as 0.5% [19].Patients with TTP have a severe deficiency of Von Willebrand Factor (VWF) cleaving metalloproteinase (ADAMTS-13), which normally cleaves the unusually large VWF into smaller and less adhesive VWF resulting in micro vascular thrombosis and thrombocytopenia when deficient, Connective tissue disorders like SLE have low levels of ADAMTS-13 suggesting a possible common Pathophysiology for this disease association [20].

In this study it has been shown that oral vesicles and bullai were found in 10 % of SLE patients, bullous lesions can occur in SLE as a subepidermal blistering disease [21], or when severe edema and hydropic degeneration occur in the basal layer. The latter condition is considered a lupus erythematosus (LE)-specific lesion [22].The former condition is a rare disorder characterized by tense fluid-filled vesicles and bulla, with an erythematous or urticarial background. Bullous SLE is a rare, transient autoimmune bullous disease that occurs in established cases of SLE [23].It appears in less than 5% of patients with SLE, either in isolation or in

addition to other cutaneous manifestations, this condition usually affects young females [24].

The reduction in salivary gland function as measured by saliva flow rate in SLE patients result from that the salivary gland are major target organs of SLE. Reduced salivary flow rate and the concomitant reduction of oral defense systems may cause severe caries and mucosal inflammations [25].

One study found that there is association between dental caries and pneumonia in patients with systemic lupus erythematosus (SLE), also found that there is an impaired salivary flow rate in SLE patients, which is considered a risk factor for dental caries [26]

Other study found that the medians of the PI and the GI were higher in JSLE patients than in controls (61.5 versus 38.10, P = 0.003 and 26.0 versus 15.95, P = 0.014; respectively) [27]. another study reported an incidence of periodontitis in 94% of patients with SLE [5], and another case showed 18 of the 30 patients (60%) had periodontitis in their SLE group [28]. to understand the reasons for the observed sialochemical changes in SLE, the process of saliva production needs to be studied closely. Under normal circumstances, primary saliva is secreted into the acinar lumen and subsequently transported to the oral cavity through the salivary ducts by contraction of epimyoepithelial cells and other hydrostatic forces. As primary saliva traverses the striated ducts, salivary composition is modified considerably: phosphate is thought to be slightly concentrated, whereas sodium and chloride are extensively reabsorbed at low flow rate [29].

Duct cells may impair in their function by the periductal lymphocytic infiltration that is present in the major salivary glands affected by the autoimmune disorder; perhaps, locally produced autoantibodies directed against duct cells cause impairment of electrolyte transport in duct cells [30].

The salivary changes observed in systemic lupus erythematosus patients reflect impaired ductal salt re-absorption; the results of this study suggest that changes in salivary flow rate, pH and salivary composition as well as increase dental caries experience in those patients may serve as potential markers of the extent of auto immune mediated salivary gland dysfunction which is similar to Sjögren's syndrome.

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