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**Oral Manifestations and Gene Polymorphism in
Systemic Lupus Erythematosus Patients with Oral
Ulcerations in Relation to Serum CD34 and Vascular
Endothelial Growth Factor**

A thesis submitted to the Council of College of Dentistry, Baghdad
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ABSTRACT

Background: Systemic lupus erythematosus is a chronic autoimmune disease with a highly variable course and prognosis, may involve several tissues and organs. Oral ulceration is one of the important symptoms in systemic lupus erythematosus. The exact etiology of systemic lupus erythematosus is unknown, it may involve many factors, one of them is genetic susceptibility; the genetic elements has a crucial role in disease etiology as there are different genes contributing in disease pathogenicity. And most of genetic missense variants were including single nucleotide polymorphisms, which associated within immunity related genes.

Aims of the study: This study was designed to evaluate the oral findings of systemic lupus erythematosus patients and correlate it to serum vascular endothelial growth factors and cluster of differentiations 34 changes and molecular investigations of some genes polymorphisms associated with oral ulcers phenotype in SLE patients; ABHD6 gene (SNPs rs9311676), UHRF1BP1 gene (SNPs rs9462027) and IKZF1 gene (SNPs rs4917014) and compare with healthy control group.

Subjects, Materials and Methods: This study was performed in Mirjan teaching hospital in Hilla city, Babylon (Rheumatology unit) during the period from 2nd May 2018 till January 2019, the sample was divided into two groups:-

Fifty two SLE patients and thirty one healthy control subjects, with no signs or symptoms of any systemic diseases.

All patients and control subjects were orally examined using disposable dental mirror and artificial portable light. About five milliliters of venous blood were taken from each subject. The blood sample was divided into two parts: about two milliliters was collected into tubes containing ethylene diamine tetra acetic acid to be used for molecular

analysis, while the other part of the blood sample was allowed for clotting at room temperature and then centrifuged for five minutes at 4000 round per minutes, the serum stored frozen at -20 °C in polyethylene tubes until analyzed. Serum was used to estimate human vascular endothelial factors-A and cluster of differentiations 34 using Sandwich-enzyme-linked immunosorbent assay principle.

Genomic DNA from blood samples of both control subjects and patients was extracted by using DNA extraction kit (Favorgen/Korea) and then by using polymerase chain reaction and spectrophotometers (Nandrop). Separation, identification and purification of DNA fragments for each gene involved in this study done by polymerase chain reaction and electrophoresis through agarose gel as a standard method. The DNA sequencing was done to all investigated gene SNPs by Macrogen Company (South Korea).

Results: The age range of Systemic lupus erythematosus patients was (15-51) years and the mean (30) years. Female to male ratio was 13:1 with significant differences. Disease duration range was (3-25) years, the mean was (9.6) years, (44.2%) of patients, were treated with rituximab, (44.2%) with Endoxan , and (11.5%) were treated with methotrexate. Oral ulceration was found in only (46.15%) of patients and no other oral findings were found, a single oral ulcer seen in (45.83%) patients, while multiple oral ulceration seen in (54.17%) patients, pain associated with oral ulcer was found in 37.5% of patients, while 62.5% were of non-painful ulceration, the tongue, labial mucosa and buccal+labial mucosa were more frequent than other sites, with highest percentage of patients were presented with tongue ulcer (20.8%). Malar rash was present in only (13.4%) patients. Serum vascular endothelial growth factor level was significantly higher in patients compared in control, while the cluster of differentiations 34 was significantly decreased in patients than in control

subjects . No significant differences were found in the level of serum vascular endothelial growth factors and cluster of differentiations 34 in patients with oral ulceration or without. For ABHD6 gene rs9311676 SNP, no significant difference were found in genotyping distribution between control subjects and patients and between patients with oral ulcer and patients without oral ulcer in alleles T and C .In UHRF1BP1 gene (rs9462027) SNP, a highly significant differences was found in genotyping distributions and in allele's frequency between patients and control subjects. Also in IKZF1 gene rs4917014 SNP a significant difference was found between patients and control subjects. Finally for cluster of differentiations 34 gene, significant differences were found between patients and control subjects in different haplotypes (A, D, E, F, G, and H). Also significant difference was found between patients with oral ulceration and patients with out in only haplotypes C and F.

Conclusions: Oral ulcers present in about half of systemic lupus erythematosus Iraqi samples, most clinically were systemic lupus non-specific oral ulcerations, mutation in genes associated oral ulcer phenotyping was important in prediagnosis and follow up as there were close association. Serum level of vascular endothelial growth factors was elevated in patients, while serum cluster of differentiation34 was reduced.