

## Original Article

### Comparison of Serum Autoantibodies to Desmogleins I, III in Patients with Oral Lichen Planus and Healthy Controls

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#### ABSTRACT

**Background & Objective:** Lichen planus is a mucocutaneous disease which is relatively common and in 30-70% of patients, mucosal lesions can be seen and known as a precancerous lesion but its etiology is not completely understood. Desmogleins I and III are the main desmosomal transmembrane proteins. These proteins have been identified as the autoantigen of the autoimmune disease. The aim of this study was evaluation of serum autoantibodies against desmogleins I, III in oral lichen planus.

**Methods:** We attempted to determine the etiology of this disease with evaluation of these serum factors. Thirty-five patients with oral lichen planus and 35 healthy controls were recruited and tested for serum autoantibodies against desmogleins I, III and indirect immunofluorescence also performed. Data were analyzed by statistical-analytical methods (Independent sample t-test) with using the SPSS.15 software.

**Results:** Serum autoantibody against desmoglein I had no significant difference in the two groups ( $P=0.31$ ) but significant increase in serum autoantibody to desmoglein III was found in patients with oral lichen planus ( $P=0.00$ ).

**Conclusion:** It seems that autoantibody against desmoglein III has a significant role in the pathogenesis of oral lichen planus.

**Keywords:** Lichen Planus, Desmogleins I, III, Serum Level

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## Introduction

Oral lichen planus (OLP) is an autoimmune mucocutaneous disorder with lymphotoxic processes against the epidermal basal keratinocyte layer as an apoptotic mechanism (1). Keratinocytes are believed to express an antigen in lichen planus; however, the nature of the antigen is unclear (2).

Eversole reported that oral mucosal erosive-ulcerative or bullous lesions involve immunopathological processes that account for the loss of adhesion among contiguous keratinocytes or to structures within the basal lamina. Antigenic triggers and molecular targets contain desmosome and hemidesmosome as anchoring elements, and basement membrane (3).

Desmogleins (DSG) I and III are restricted to stratified epithelium. DSGI is more intensively expressed as the cells differentiate toward the stratum corneum and is barely detectable in the basal layer, but DSGIII is localized to the basal and suprabasal layers (4).

Lukac *et al.* reported that humoral autoimmunity seems to be involved in the pathogenesis of oral lichen planus. The differences in concentrations of desmoglein serum autoantibodies suggested that the pathological mechanisms in erosive and reticular forms of oral lichen planus may not be the same (5).

However, in some previous studies it was suggested that these antibodies (IgG) were present in low titers and were not specific to a particular clinical presentation of lichen planus or lichenoid drug reaction. Therefore, they speculated that such antibodies are not as a part of etiopathogenesis in lichen planus (6).

Most of the characteristics were consistent with those reported in previous studies, while a few were not in agreement with those studies (7). Therefore, the purpose of the present study was to determine the presence of circulating au-

toantibodies to desmoglein (Dsg) I and Dsg III in Iranian patients with OLP. The effects of these specific cell-to-cell interactions were also hypothesized.

## Material and Methods

In this case-control study which conducted in 2011, 35 cases of OLP without cutaneous lesions were selected based on clinical patterns and were confirmed as lichen planus by histopathological analysis in the Department of Oral Medicine at the Dentistry Faculty of Tabriz University of Medical Sciences, Tabriz, Iran. A group of healthy controls consisted of 35 apparently healthy volunteers. None of the patients suffered from any systemic disease or received any systemic or topical therapy that could influence the results of tests performed in this study.

Patients with other similar diseases, such as pemphigus, mucous membrane pemphigoid, erythema multiform, and lupus erythematosus, were excluded.

Informed consent according to the Helsinki Declaration II was obtained from each individual before the study (8), and the study was approved by the Ethics Committee of the School of Dental Medicine of the university.

Peripheral blood for the determination of circulating autoantibodies was drawn from each participant between 8 a.m. and 9 a.m. A commercial enzyme-linked immunosorbent assay (ELISA, Cusabio Company) was used to determine autoantibodies to both desmogleins I and III. An indirect immunofluorescence test was also performed with monkey esophagus epithelium kits manufactured by Euroimmun. Simple sampling methods were performed with patients referred to the same center in the 9-month period.

## Equipment

Measurement tools were desmoglein I and III

kits, obtained from Cusabio, ELISA kits (CSB-E13894h human desmoglein I IgG antibody ELISA kit and CSB-13896h human desmoglein III IgG antibody ELISA kit), and monkey esophagus epithelial tissue, obtained from Euroimmun, for indirect immunofluorescence (IIFT Epidermis-esophagus, Code No. FA 1501-1005).

### Detection of Autoantibodies

For the determination of autoantibodies in ELISA kits, antibodies against human autoimmune antibodies were attached to the bottom of each row of the plate. Samples included standard desmoglein I and III autoantibodies diluted 1:100, and serum samples from both patients and controls. The pooled samples were poured into the wells. During the first incubation, desmogleins I and III bound to the antibody were fixed and washed, after which the specific antibody binding to desmogleins I and III was added. During the second incubation, the antibody against desmoglein I and III autoantibodies, still attached from the first incubation, was washed, after which horseradish peroxidase (HRP) was added to the antibody, which bound to the attached biotin. After the third incubation and washing of unbound enzyme, tetramethylbenzidine (TMB) was added, and the fourth stop was added after incubation. Results were read at 450 nm.

### Indirect Immunofluorescence Assay

A standard indirect immunofluorescence assay with monkey esophagus tissue as substrate was carried out to determine autoantibodies to epithelial antigens in participants' sera. Fluorescein isothiocyanate-conjugated goat anti-human IgG specific for gamma chains was used as the second antibody. Patients' sera were screened at a dilution of 1:20 in phosphate-buffered saline.

### Statistical Analysis

Data obtained from the study were analyzed

by descriptive statistics (mean  $\pm$  SD) and mean comparison tests for independent groups and the independent-samples *t*-test with SPSS.15 software. Statistical analyses were studied, and the results compared with those from the Mann-Whitney U test were used for indirect immunofluorescence. The significance level was set at 0.5, and  $P < 0.05$  was considered statistically significant.

## Results

Among the participants in the study, there were 35 healthy individuals and 35 patients with OLP. Among these, 42 patients (60%) were female and 28 (40%) were male.

The concentrations of serum autoantibody against desmoglein I were not significantly different in the two groups ( $P= 0.31$ ), but a significant increase in the concentration of serum autoantibody to desmoglein III was found in patients with OLP ( $P= 0.00$ ) (Table 1). Indirect immunofluorescence analysis with monkey esophagus epithelium showed significantly more findings positive to epithelial structures in patients with OLP (30 positive of 32 tested) than in the healthy group (Table 1). There was no difference in indirect immunofluorescence findings between the patients with OLP and healthy controls (Table 1).

## Discussion

In the present study, serum autoantibody against desmoglein I showed no significant difference in the two groups, but a significant increase in serum autoantibody to desmoglein III was found in patients with OLP.

Increased concentrations of anti-desmoglein III autoantibodies, detected in the sera of patients with OLP, indicated that anti-keratinocytes to autoantibodies may be involved in the pathogenesis of OLP. The presence of desmoglein III in connection with mucosal tissue cells and

**Table1-** Characteristics, serum concentrations of autoantibodies to desmoglein 1 and 3, and indirect immunofluorescence findings in 70 patients with oral lichen planus and healthy controls

Characteristic	Oral lichen planus (n=35)	Controls (n=35)
Age (median, range;y*)	43.7(23-60)	38(23-40)
Sex (M**/F***)		
Autoantibodies	15.20	13.22
(U/mL,median,interquartile range)	0.32(0-2.1)	0.31(0-1.6)
anti-Dsg***I	6.9(0-15.6)	0.83(0-2)
anti-Dsg III	30.32	2.20
IIF****(Positive/Tested)		

\*: Years

\*\*: Male\*\*\*: Female

\*\*\*\*: Desmogelin

\*\*\*\*\*: IndirectImmunofluorent

desmoglein I in connection with dermal cells plays a main role (2). In this study, we excluded patients with cutaneous lichen planus, which could explain this result.

Munde *et al.* described the epidemiological and clinical characteristics of patients with OLP in a relatively small cohort of the rural population in India Most of the characteristics were consistent with those described in previous studies, while a few were not in agreement with those studies. Therefore, it seems that geographic variance could affect the demographic and clinical presentation of OLP (7).

Lukac and colleagues studied 57 Croatian patients with OLP and found that concentrations of serum antibodies against desmogleins I and III in patients with non-erosive forms of lichen planus, erosive forms of lesions (reticular, bullous), and in a control group of patients with recurrent acute aphthous ulcers showed a significant increase (5). These authors showed that the humoral immunity against keratinocyte cadherins desmogleins I and III seems to play a role in OLP. They had chosen recurrent aphthous ulceration and OLP because these seemed to share the immunopathological features involving T-cell-mediated immunity. They also included in the study patients who were taking medications. Medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) can cause lichenoid reactions. These authors did not report whether concomitant cutaneous lichen

planus was present. Therefore, the results of their research cannot be extrapolated.

In our study, we did not classify the patients with lichen planus, because of the major role of desmoglein III in connection with mucosal cells. The presence of elevated serum autoantibodies against desmoglein III in patients with OLP is more reasonable.

## Conclusion

Due to the dearth of studies in this area, we were unable to compare our results with those of other studies. Our study supports the crucial role of DsgIII for keratinocyte cohesion and epidermal integrity in OLP.

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