



## Original Research Article

## Role of serum immunoglobulins in patients of oral lichen planus and oral lichenoid reaction

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## ARTICLE INFO

## Article history:

Received 07-05-2020

Accepted 16-07-2020

Available online 28-09-2020

## Keywords:

Humoral immunity

IgA

IgM

Oral lichen planus

Oral lichenoid reactions

## ABSTRACT

**Introduction:** The aim of the study is to find out the role of immunoglobulin IgA and IgM as indicators of humoral immune response in the etiopathogenesis and for the differentiation between oral lichen planus (OLP) and oral lichenoid reaction (OLR).

**Materials and Methods:** The study comprises of 50 patients. From them 20 patients were of OLP, 20 patients of OLR and 10 patients as controls. After histopathological confirmation, approximately 5 ml of venous blood was collected by venepuncture from OLP patients, OLR patients and from control patients. The serum IgA and IgM were measured by immunoturbidimetry method using automated chemistry analyzer and data were analysed using t-test.

**Results:** The mean serum level of IgA and IgM was  $2.14 \pm 1.19$ g/L and  $0.88 \pm 0.47$ g/L respectively in reticular OLP,  $2.21 \pm 0.98$ g/L and  $0.78 \pm 0.49$ g/L respectively in erosive OLP,  $1.64 \pm 0.60$ g/L and  $0.99 \pm 0.34$ g/L respectively in OLR,  $2.62 \pm 0.40$ g/L and  $1.51 \pm 0.47$ g/L respectively in control patients. The results showed statistically significant IgM level for reticular and erosive OLP (p value=0.007 and 0.042 respectively).

**Conclusion:** Patients with OLP shows systemic immunologic alterations suggest that humoral immune system may play a part in pathogenesis of OLP and also OLP and OLR lesions can be differentiate on the basis of serum level of IgM.

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## 1. Introduction

Oral Lichen Planus (OLP) is a relatively common potentially malignant disorder and chronic dermatologic disease that affects the oral mucosa.<sup>1</sup> It is confirmed that different causes participate in its pathogenesis yet etiology is not well established. Immunologic mechanisms are widely accepted as one of the potential factors in the pathogenesis of OLP.<sup>2</sup>

Clinically and histologically, Oral lichenoid reactions (OLR) are similar to Oral lichen planus lesions. These may involve skin or oral mucosa. But unlike lichen planus the underlying cause is identifiable and withdrawal of the same leads to remission of these lesions.<sup>3</sup> Dental restorative

materials, flavouring agents, graft-versus-host disease, tobacco chewing and some medications are triggering factors in the causation of Oral lichenoid reactions.<sup>4</sup>

Immunoglobulins (Ig) are glycoproteins which are expressed as membrane bound receptors on the surface of B cells or soluble molecules secreted from plasma cells which are IgG, IgA, IgM, IgD and IgE. In normal serum, IgA is second most predominant immunoglobulin whereas IgM is the first antibody to appear in the response to initial exposure to an antigen. This study was designed to quantitatively evaluate IgA and IgM in serum, thereby to observe association of IgA and IgM in the pathogenesis of OLP and OLR.<sup>5</sup>

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## 2. Materials and Methods

The study comprises of 50 patients. From them 20 clinicopathologically proven oral lichen planus patients of which 7 were males and 13 were females and 20 clinicopathologically proven oral lichenoid reaction patients of which 6 were males and 14 were females. A group of 10 age matched healthy patients included as controls in which 5 were males and 5 were females.

Hospitalized patients and patients having autoimmune disorders were excluded. Ethical clearance for the study was obtained from the Institutional Ethical Committee and Review Board. The patients were explained regarding the study procedure and written consent was obtained.

From all the lesional patients except controls, the punch biopsy was collected, tissue was fixed in 10% neutral buffered formalin immediately, routinely processed, embedded in paraffin wax, 4-5  $\mu\text{m}$  thick sections were cut and slides were prepared for routine Haematoxylin and Eosin stain to carry out histopathological diagnosis of OLP and OLR. After histopathological confirmation, approximately 5 ml of blood was collected by venepuncture from the antecubital vein from the patients having OLP and OLR and from control patients and then immediately placed into serum separator vacutainer. The blood sample was allowed to clot for 30 minutes before separating the serum. After centrifugation for 10 minutes at approximately 3000 rpm, the serum was separated and stored at  $-80^{\circ}\text{C}$  until analysis. IgA and IgM was measured using immunoturbidimetry method using automated chemistry analyzer.

The normal serum level of IgA and IgM is 0.7-4.0 g/L and 0.4-2.3 g/L respectively. The data obtained was tabulated and statistically analysed using statistical package for social science (SPSS version 20.0). All the data obtained were subjected to Student t-test and analysis of variance (ANOVA) for comparison of data.

## 3. Results

The present study comprised of a total 50 patients. From them, 16 patients with reticular OLP had mean serum level of IgA was  $2.14 \pm 1.19 \text{g/L}$  and IgM was  $0.88 \pm 0.47 \text{g/L}$ . 4 patients with erosive OLP had mean serum level of IgA was  $2.21 \pm 0.98 \text{g/L}$  and IgM was  $0.78 \pm 0.49 \text{g/L}$ . 20 patients with OLR had mean serum level of IgA was  $1.64 \pm 0.60 \text{g/L}$  and IgM was  $0.99 \pm 0.34 \text{g/L}$ . 10 control patients had mean serum level of IgA was  $2.62 \pm 0.40 \text{g/L}$  and IgM was  $1.51 \pm 0.47 \text{g/L}$  as shown in Table 1. The results showed that IgM level was statistically significant for reticular OLP ( $p$  value=0.007) and erosive OLP ( $p$  value=0.042). The above findings suggests that mean serum level of IgA and IgM of OLP and OLR patients was lower than controls but was within normal range. The mean serum level of IgA in patients with OLP was higher as compared to patients with OLR where mean

serum level of IgM was lower in OLP patients as compared to OLR patients.

In the present study, out of 16 patients of reticular lichen planus, mean serum levels of IgA and IgM in males was  $2.49 \pm 1.75 \text{g/L}$  and  $1.32 \pm 0.50 \text{g/L}$  respectively and in females it was  $1.98 \pm 0.90 \text{g/L}$  and  $0.68 \pm 0.30 \text{g/L}$  respectively where the IgM level was statistically significant ( $p$  value=0.006). In 4 patients of erosive OLP, in males mean serum levels of IgA and IgM was  $2.35 \pm 0.63 \text{g/L}$  and  $0.41 \pm 0.40 \text{g/L}$  respectively and in females, it was  $2.08 \pm 1.55 \text{g/L}$  and  $1.15 \pm 0.09 \text{g/L}$  respectively. In 20 patients of OLR, in males mean serum levels of IgA and IgM was  $2.17 \pm 0.46 \text{g/L}$  and  $1.28 \pm 0.33 \text{g/L}$  respectively and in females, it was  $1.41 \pm 0.53 \text{g/L}$  and  $0.87 \pm 0.29 \text{g/L}$  respectively which is shown in Table 2. Thus present findings suggests that mean serum level of IgA was slightly decreased while IgM level was considerably decreased in females with comparison to males in reticular OLP but serum level of IgA was slightly decreased and IgM was considerably increased in females with comparison to males in erosive OLP while in OLR, mean serum level of IgA and IgM was increased in males with comparison to females.

## 4. Discussion

OLP is usually a self limiting condition of unknown etiology and for that several hypothesis are put forward but no satisfactory answers is found for its etiology. An immune mechanism was suggested by various researchers where they have reported its association with several autoimmune disorders.<sup>6</sup> The cause of lichen planus is unknown; however, an immunologic component may exist. Researchers have shown the role of serum IgG, IgA and IgM in patients with OLP.<sup>7</sup> Immunoglobulins are responsible for humoral immunity. Every increased or reduced value of certain immunoglobulins is an indicator of the existence of some morbid process and the degree of its activity not dependant on its location and specificity.<sup>2</sup> The etiology of OLP is still under discussion with a tendency to autoimmunity while etiology of OLR is known and is related to the contact with specific antigens where OLR is caused by the antigen fixation in the epithelial cells which are recognized and destructed by the cells of the immune system. The immunoglobulins and autoantibodies play the key roles in multicausal pathogenesis of OLP.

In present study, there was decrease in the mean serum level of IgA in patients with reticular OLP and erosive OLP with comparison to controls but was within the normal range. Findings of the present study were quite correlated with the findings of Rodriguez Nunez et al (2001), Scully (1981), Jacyk and Greenwood (1978) and Griffith et al (1974). Rodriguez Nunez et al (2001) reported that in all cases of OLP mean values were within the corresponding general population normal ranges.<sup>8</sup> Jacyk and Greenwood (1978) found that mean serum levels of IgA

**Table 1:** Comparison of mean serum levels of IgA and IgM in patients with OLP, OLR and control

Lesions	No. of Patients	IgA (g/L)			IgM(g/L)			
		Mean	SD	P value	Mean	SD	P value	
Oral Lichen Planus	Reticular	16	2.14	1.19	0.550	0.88	0.47	0.007
	Erosive	4	2.21	0.98	0.870	0.78	0.49	0.042
Oral Lichenoid Reaction	-	20	1.64	0.60	0.086	0.99	0.34	0.064
Control	-	10	2.62	0.40	-	1.51	0.47	-
Total	-	50	-	-	-	-	-	-

**Table 2:** Sex wise comparison of mean serum levels of IgA and IgM in patients with OLP and OLR

Lesions	No. of Patients	Male				Female				
		IgA(g/L)		IgM(g/L)		IgA(g/L)		IgM(g/L)		
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Oral Lichen Planus	Reticular	16	2.49	1.75	1.32	0.50	1.98	0.90	0.68	0.30
	Erosive	4	2.35	0.63	0.41	0.40	2.08	1.55	1.15	0.09
Oral Lichenoid Reaction	-	20	2.17	0.46	1.28	0.33	1.41	0.53	0.87	0.29
Total	-	40	-	-	-	-	-	-	-	-

**Table 3:** Independent sample T-test

Lesional group	Immunoglobulins	Sex	No. of Patients	Mean	Mean Difference	P Value
Reticular OLP	IgA	Male	5	2.49	0.51	0.443
		Female	11	1.98		
	IgM	Male	5	1.32	0.64	
		Female	11	0.68		
Erosive OLP	IgA	Male	2	2.35	0.27	0.840
		Female	2	2.08		
	IgM	Male	2	0.41	-0.74	
		Female	2	1.15		
Oral Lichenoid Reaction	IgA	Male	6	2.17	0.76	0.063
		Female	14	1.41		
	IgM	Male	6	1.28	0.41	
		Female	14	0.87		

and IgM were similar in patients and controls.<sup>7</sup> Whereas Biocina- Lukenda et al (2008) noted significantly increased mean serum levels of IgA and IgM in OLP patients with comparison to healthy controls.<sup>9</sup> They concluded that humoral immunity plays a role in the pathogenesis of OLP where significantly elevated serum IgA and IgM might indicate emergence of defence mechanisms starting from the local level and might suggest that this immunological mechanism is attempt to eliminate bacterial antigen as possible etiological factor in the development of OLP.<sup>7,8,10,11</sup>

There was decrease in the mean serum level of IgM in reticular OLP patients and erosive OLP patients with comparison to controls in the present study but it was within the normal range and was statistically significant (p=0.007 and p=0.042) respectively. This was quite correlated with

the findings of Rodriguez Nunez et al (2001), Jacyk and Greenwood (1978) and Griffith et al (1974) whereas Ghaleyani et al (2012) concluded no significant difference in salivary levels of IgA and IgM as compared to controls in OLP patients and OLR patients which was correlated with the present study.<sup>7,8,11,12</sup> The findings of Griffith et al (1974) was not correlated with the present study who noted that there were no consistent abnormalities in serum immunoglobulins which might account for oral lesions of lichen planus.<sup>11</sup>

The high IgA values observed in some patients with erosive lesions may reflect secondary infection. Because these elevated levels were not present in all patients with erosive lesions and because the serum values for nonerosive patients were normal, it is assumed that serum immunoglobulins were not primarily involved in lesion

production. Also the study by Biocina-Lukenda et al (2008) and Lundstrom (1985) showed increased serum levels of IgA which was statistically highly significant as compared to controls which was not in accordance with present findings whereas Popovska et al (2014) and Stankler (1975) showed significantly decreased serum levels of IgA and IgM in OLP patients which was somewhat correlated with present findings where the IgM level was significantly decreased.<sup>2,9,13,14</sup> In present study, mean serum level of IgA was decreased in females with comparison to males which was in accordance with the findings of Lundstrom (1985).<sup>13</sup> The mean serum level of IgM in females was significantly decreased with comparison to males in present study but Lundstrom (1985) noted increased IgM levels but was within normal limits.<sup>13</sup> Whereas the study by Griffith et al. (1974) found low values of mean serum level of IgA and IgM in females with comparison to males.<sup>11</sup> The results of different studies of serum immunoglobulins in lichen planus patients are highly contradictory. In present study, mean serum level of IgA was within the corresponding normal range. We detected statistically significant differences of mean serum levels of IgM in patients with reticular and erosive OLP compared to controls. This hold up the view that patients with OLP show systemic immunologic alterations and that the humoral immune system may play a part in pathogenesis of OLP and we can differentiate OLP and OLR lesions on the basis of serum level of IgM. In present study, there was statistically significant difference noted in the mean serum levels of IgM between male and female in reticular OLP patients. In females it was considerably decreased with comparison to males so we can justify the higher occurrence of OLP lesions in females with comparison to males.

## 5. Conclusion

The differential diagnosis is difficult between OLP and OLR as clinicians are unaware of these diseases or who do not follow their patients for the period required for their differentiation or microscopic diagnosis of OLR may not be reached due to lack of indication of cause-effect relationship. From the above study, we can differentiate between OLP and OLR lesions on the basis of serum level of IgM as humoral immunity may play a part in the pathogenesis of OLP. The final diagnosis should be made as early as possible because there is different treatment for both OLP and OLR and OLP should be more carefully followed due to possibility of malignant transformation.

## 6. Source of Funding

None.

## 7. Conflicts of Interest

None

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**Cite this article:** Gajjar N, Peddiwar V, Prajapati M. Role of serum immunoglobulins in patients of oral lichen planus and oral lichenoid reaction. *Int J Clin Biochem Res* 2020;7(3):384-387.