

# Elevated Estrogen Levels in Patients with Oral Lichen Planus- A Pilot Study

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## Abstract

**Background :** Lichen planus is a T-cell mediated autoimmune disease. Autoimmune diseases are chronic conditions initiated by the loss of immunological tolerance to self-antigens and represent a heterogeneous group of disorders. Estrogen, testosterone and progesterone have significant biological actions that can affect other organ systems including the oral cavity.

**Methodology :** The current study assessed the serum estrogen and testosterone levels in patients with oral lichen planus. 10 patients, 5 patients with clinical presentation of oral lichen planus and 5 normal healthy individuals or patients with oral lichenoid reaction visiting the Department Of Oral Medicine and Radiology at ITS-CDSR Muradnagar were selected. 5ml of blood sample was withdrawn from each patient. Enzyme linked fluorescence assay was performed using TOSOH AIA 360 technique for evaluation of estrogen and testosterone levels. **Results :** Increased estrogen levels was observed in patients with oral lichen planus. Testosterone level was within normal range in oral lichen planus and patients with lichenoid reaction.

**Conclusion :** Autoimmunity as evidenced by increase levels of estrogen could be one of the etiological factor of oral lichen planus.

**Key words :** Oral Lichen Planus, Oral Lichenoid Reaction, Estrogen, Testosterone.

## Introduction

Oral lichen planus (OLP) is a chronic inflammatory disease affecting any part of the mucous membrane of the oral cavity. It is a T-cell mediated autoimmune response in which the cytotoxic CD8+ T cells triggers apoptosis of the basal cells of oral epithelium. There are several antigen-specific and nonspecific inflammatory mechanisms that have been put forward to explain the accumulation and homing of CD8+ T cells subepithelially and also the subsequent keratinocyte apoptosis.<sup>1</sup>

The classic skin lesions of the cutaneous form

of lichen planus can be described with 5 Ps as purplish, polygonal, planar, pruritic papules and plaques. There are several types of OLP that have been described in the literature but the two main types are reticular and erosive lichen planus.<sup>2</sup>

Oral lichenoid reactions are also considered as the variants of oral lichen planus but they may be regarded as a disease by itself. They can also be regarded as exacerbations of existing oral lichen planus by the presence of medications or dental materials.<sup>3</sup>

Autoimmune diseases represent a heterogenous group of disorders that afflict

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the specific target organs or the multiple organ systems. The chronic nature of these diseases places a significant burden on the utilization of medical care, direct and indirect economic costs, and the quality of life. Almost all the autoimmune diseases affect the middle aged women and are amongst the leading causes of death. With the increasing age of the patients, the female-to-male ratio for the autoimmune diseases also becomes more prominent.<sup>4</sup>

Sex hormones seem to play a major role as the modulators of autoimmune diseases' onset/perpetuation. Generally, the steroid hormones are implicated in the immune response, estrogens as enhancers and androgens and progesterone as natural immunosuppressors.<sup>5</sup> Estrogen and progesterone have significant biological actions that can affect organ systems including the oral cavity. Receptors for the estrogen and progesterone have also been demonstrated in the gingiva which can be thought of as a target organ for progesterone and estrogen. Estrogen receptors are also found on the periosteal fibroblasts, scattered fibroblasts of the lamina propria, and also the periodontal ligament fibroblasts and osteoblasts.<sup>6</sup>

It is still unknown if lichen planus represents a single disease process or several closely related entities with similar clinical presentations.<sup>7</sup>

A few studies like "Effect of hormonal level in patients with diabetes type 1" by Christine Maric et al in 2010, Rheumatoid arthritis by Cutolo M et al in 2004, Effect of hormonal change on gingival tissues by Eleni Markou et al in 2009, Periodontal tissues by G.N Guncu et al in 2005 have been done. But no studies have been reported in the literature on the estimation of estrogen and testosterone level

in patients with oral lichen planus as indicators of underlying autoimmunity. With this background, a study was conducted to evaluate the role of auto-immune mechanism by disturbances in hormonal levels mainly estrogen and testosterone, in an effort to distinguish between lichenoid reaction and true lichen planus.

### Methodology

A Study was conducted in the department of Oral Medicine and Radiology at ITS- CDSR Muradnagar, Ghaziabad. A total of 10 consecutive patients were selected from those visiting the department of Oral Medicine and Radiology in the month of May-June 2013. These patients were not age and sex matched. Medically compromised patients, patients already on corticosteroids and pregnant and lactating mothers were excluded from the study. Selected patients were then divided into 2 groups (5 patients in each group). The study group included patients with clinical presentation of any type of oral lichen planus. The control group constituted healthy patients or patients with clinical presentation of oral lichenoid reaction. Patients were informed prior to beginning of the study and a written consent form was obtained. Ethical clearance was obtained from the institutional Ethical Committee. Proper dental and medical history were recorded. Thorough clinical examination was done for each patient. 5ml of blood sample was withdrawn and was sent to the laboratory. Enzyme linked Immunofluorescence Assay was performed using the Fluorescence Enzyme Immunoassay By TOSOH AIA 360. Levels of estrogen and testosterone were estimated and then evaluated.

Expected values of total testosterone : In females: Follicular Phase 00 – 118, Midcycle

21 – 104, Luteal Phase 00 – 119, Oral Contraceptives 00 – 110, Postmenopausal 00 – 80 In males :(20-53 years) 262-1593.

Expected values of estrogen : In males: 11.6 - 41.2 pg / ml. In females: Follicular Phase (+ 4 to + 12 Days) 18.9 - 246.7 pg / ml, Mid cycle (+ 4 to + 12 Days) 35.5 - 570.8 pg / ml, Luteal Phase (+ 4 to + 12 Days) 22.4 - 256.0 pg / ml and Post-Menopausal Phase - 44.5 pg / ml.

### Results

A total of 10 consecutive patients visiting the department of Oral Medicine and Radiology at I.T.S-CDSR, Muradnagar in the month of May-June 2013 were selected. Male: female

was 9:1. These patients were not age and sex matched. Age range was 20-66 years (mean= 43 years). In the study group, patients presented with plaque, reticular and erosive type of lichen planus. Increased estrogen (E<sub>2</sub>) level was observed in all patients in the study group (Table 1). Based on clinical presentation, 5 patients were included in the control group of oral lichenoid reaction. Estrogen level was found within normal range in all the patients in control group (Table 2). Testosterone level was observed within normal range in both the study and the control group.

**Table-1 : Study group showing increased estrogen level in patients with oral lichen planus. Testosterone level is within range.**

S.NO	Age/sex	Testosterone (ng/dl)	Estradiol (E2 ) (pg/dl)	Type of lichen planus
1	22/M	357	56	Plaque type lichen planus
2	42/M	651	54	Reticular lichen planus
3	66/M	679	68	Erosive lichen planus
4	38/M	661	45	Reticular lichen planus
5	40/M	482	89	Reticular lichen planus

**Table-2 : Control group showing estrogen and testosterone level within range in patients with oral lichenoid reaction.**

Age/sex	Testosterone (ng/dl)	Estradiol (E2 ) (pg/dl)
40/F	67	23
20/M	809	29
32/M	328	21
58/M	475	21
23/M	634	31

## Discussion

Generally, steroid hormones are the mediators of immune response, with estrogens as enhancers, androgens and progesterone as the natural immunosuppressors.<sup>5</sup>

In a study by Cutolo M et al in 2004, serum levels of estrogens have been found to be altered in rheumatoid arthritis (RA) and Systemic Lupus Erythematosus (SLE) patients, particularly in man.<sup>8</sup> OLP is a chronic autoimmune mucocutaneous disease that affects oral mucosa besides skin, genital mucosa, scalp and nails. An immune mediated pathogenesis have been recognized in OLP, although the exact etiology is still unknown.

Oral lichenoid reactions are considered as the variants of OLP and may be regarded as a disease by itself or an exacerbation of an existing OLP.<sup>3</sup> In a previous study by Cutolo M et al 2003, the synovial fluid levels of proinflammatory estrogens relative to androgens are significantly elevated in both males and females with rheumatoid arthritis, as compared to the control group which is most probably due to an increase in the local enzymatic aromatase activity. Increased estrogen concentrations have been observed in rheumatoid arthritis patients. Synovial fluid of both sexes are characterized mainly by the hydroxylated forms, in particular, 16 alpha-hydroxyestrone, which shows a mitogenic tumor growth stimulating role.<sup>5</sup> Serum hydroxylated estrogens are also found to be altered in the serum of systemic lupus erythematosus (SLE) patients. They concluded that locally increased estrogens (i.e., synovial tissue in RA or skin in SLE) might exert an activating effect on the cell proliferation, which includes macrophages and fibroblasts and suggests new roles for estrogens in autoimmunity.<sup>5</sup> Since sample size was small and statistical analysis was not performed, further studies with a larger sample size is required to be conducted for validity of the study. No studies have been done where these sex hormones have been

analysed in oral lichen planus. Hence we cannot compare our results. But this study indicates that increased levels of estrogen is observed in patients with oral lichen planus which may be one of the etiological factor.

## Conclusion

OLP is a very common oral dermatosis and one of the most frequent mucosal pathosis encountered by dental practitioners. Results show increased serum levels of estrogens in lichen planus patients. So it can be concluded that autoimmunity response can be the etiological factor of oral lichen planus. Testosterone which is an immunosuppressive hormone was not elevated, again giving indirect reflection of an underlying autoimmune response. Sample size was small, so studies with a larger sample size should be conducted for better results and validity.

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