

**DOES PROLACTIN PLAY ANY ROLE IN LICHEN PLANUS? A CASE CONTROL STUDY**Ghalaut V.S.<sup>1</sup>, Sarkar M.\*<sup>2</sup>, Dayal S.<sup>3</sup> and Samanta S.<sup>4</sup><sup>1</sup>Professor and Head. Department of Biochemistry. PT. B. D. SHARMA PGIMS Rohtak, India.<sup>2</sup>Department of Biochemistry. PT. B. D. SHARMA PGIMS Rohtak, India.<sup>3</sup>Associate Professor. Department of Dermatology. PT. B. D. SHARMA PGIMS Rohtak, India.<sup>4</sup>PDCC. Senior Resident. Department of Critical Care Medicine. SGPGIMS, Lucknow, India.

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**ABSTRACT**

**Objective:** Lichen planus (LP) is an autoimmune chronic inflammatory disease involving the skin and mucous membranes. Various cytokines are involved in etiopathogenesis of LP similar to psoriasis. Prolactin (PRL), a peptide hormone secreted from pituitary, has a key role in autoimmune related diseases like lupus erythematosus, rheumatoid arthritis and psoriasis. Prolactin may be a good biomarker of severity of disease with similar autoimmune inflammatory etiopathogenesis. So we performed the current study to evaluate serum level of prolactin in LP patients and to study any correlation of prolactin level with duration of illness. **Material and Methods:** We conducted the prospective case control study from July 2014 to June 2015 on 30 newly diagnosed patients of LP and 30 age and sex match healthy control subjects. We measured serum prolactin level by chemiluminescence technique. **Results:** Serum PRL level in total 60 subjects, 30 patients of LP and 30 age and sex matched healthy volunteers were analysed in this study. PRL level was found to be significantly higher in LP patients as compared to healthy volunteers ( $p < 0.05$ ). In mucocutaneous form of LP, PRL was found to be significantly higher compared to other forms, such as cutaneous and oral LP ( $p < 0.05$ ). Serum PRL had a positive correlation with duration of illness of LP ( $r$  value = 0.310,  $p = 0.09$ ). **Conclusion:** Hyperprolactinemia is associated with Lichen Planus. Prolactin may play a role in the pathogenesis of lichen planus. It may be a biological marker of disease activity in patients with lichen planus. Further large scale studies are needed to prove our findings.

**KEYWORDS:** Prolactin, Lichen planus.**INTRODUCTION**

Lichen planus (LP) is a common chronic inflammatory, autoimmune disease involving the skin and mucous membranes. This disease is more common in middle aged patients & females are more involved than males.<sup>[1]</sup> Clinically it presents as white striation (wickham striae), white papules, erythema, erosions or blisters.<sup>[2]</sup> Buccal mucosa, dorsum of tongue and gingiva are commonly affected.

LP has an autoimmune etiopathogenesis with involvement of various cytokines similar to psoriasis. Oral LP (OLP) is associated with T-cell mediated autoimmune disease patterns of Th1/Th2 (Helper T Lymphocyte) imbalance, Th1 or Th2 overactivation or mixed Th1/Th2 conditions, play key role in the pathogenesis of OLP.<sup>[3]</sup> Various cytokines such as IL (Interleukin)-2, IL-12, TNF (Tumor necrosis factor)- $\alpha$ , interferon (IFN)- $\gamma$  and transforming growth factor- $\beta$ 1 are involved in the pathogenesis of LP similar to psoriasis.<sup>[1]</sup>

Prolactin (PRL) a peptide hormone secreted from pituitary, has a role in autoimmune related diseases like systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and psoriasis.<sup>[4]</sup> There is limited literature on prolactin status in other dermatological disease except psoriasis. Prolactin may be a good biomarker of severity of disease with similar autoimmune inflammatory etiopathogenesis. It might have a potential role in pathogenesis in LP. To the best of our knowledge there is no previous literature on serum prolactin level in patients with LP. We hypothesised that prolactin may have role in the etiopathogenesis of LP.

So we conducted the current study to compare serum prolactin levels in recently diagnosed LP patients and healthy controls. We also evaluated the relation between prolactin levels and duration of illness.

**METHODOLOGY**

This prospective case control study was conducted in Rohtak, India from July 2014 to June 2015. Written

informed consent was taken from all subjects included in the study.

We prospectively recruited 30 new clinically diagnosed cases of LP patients, not on any treatment for last four weeks as subjects after meeting the inclusion criteria. We also selected 30 age and sex matched healthy controls from healthy hospital staffs not affected by psoriasis or other autoimmune diseases. We included our study subjects aged between 20 to 60 years.

We excluded all known cases of kidney disease, liver disease, ischemic heart disease, neurological disease, endocrine disorders, malignancy, Polycystic ovarian syndrome, pregnant or lactating women, patients undergone major surgery or trauma and subjects having drug addiction. Patients under treatment with systemic corticosteroids, lipid lowering agents, thiazides, retinoids, beta blockers, methotrexate, cyclosporine, psychotropic drugs, thyroid hormones, estrogens or contraceptives and immunosuppressive were also excluded from the study.

Serum prolactin was done before the start of treatment in LP patients. In women samples were taken during premenstrual phase of the cycle. We collected venous blood during morning time and immediately centrifuged it before analysis. Serum prolactin level was estimated by chemiluminescence (ADVIA Centaur CP immunoassay system, Siemens). Complete history and physical examination with anthropometry were also performed in cases and controls.

#### Data Collection

**Table 1: Demographic characteristics.**

Parameters	Lichen planus(n=30)	Healthy volunteers(n=30)	P value
Gender(M/F)*	18/12	16/14	0.301
Age (in year)\$	36.43 ± 12.66	38.97 ± 7.05	0.343
BMI(kg/m <sup>2</sup> )\$	26.03 ± 2.52	25.09 ± 2.07	0.121
Forms of illness	Cutaneous-16 Mucocutaneous-11 Oral-3		

\*expressed in frequency, \$ expressed in Mean ± SD.

We found significantly higher prolactin level in LP patients as compared to healthy volunteers (16.52 ± 7.67 and 11.53 ± 4.94 respectively, p<0.05; Table 2, Figure 1). In mucocutaneous form of LP, leptin was found to be significantly higher compared to other forms, such as cutaneous and oral LP (p<0.05; Table 3).

**Table 2: Serum prolactin level in two groups (Mean ± SD).**

Parameters	Lichen planus (n = 30)	Healthy volunteers (n = 30)	P value
Prolactin(ng/ml)	16.52 ± 7.67	11.53 ± 4.94	0.004*

\* means statistically significant with p value < 0.05.

Detailed history regarding all demographic parameters (age, sex, BMI, socioeconomic status, addictions, duration of disease) and any systemic illness or any drug intake were taken. Routine biochemical parameters and serum prolactin levels were measured. All relevant data were recorded.

#### Statistical Analysis

Statistical analysis was done by standard statistical software SPSS version 18 using appropriate statistical tests. Data were expressed as Mean ± SD, frequency or number as appropriate. Pearson Chi Square Test was used for categorical variables. Comparison among groups was analysed using independent student t test or Mann Whitney U test or ANOVA test as appropriate. Pearson correlation was used to examine the strength of correlation between prolactin level and duration of illness of LP. For all statistical tests P value < 0.05 was considered as significant.

#### RESULTS

A total of 60 subjects were included in the study with 30 subjects in each group comprising of patients of LP and healthy volunteers respectively. Age, gender and BMI distribution were comparable between two groups. In LP group we found different morphological variants such as cutaneous LP-16 patients, mucocutaneous LP- 11 patients, oral LP- 3 patients (Table1).

Serum prolactin had a positive correlation with duration of illness of LP (r value=0.310, p = 0.09, Figure 2).

Overall, we also found comparable serum prolactin level between high BMI than low BMI group (p >0.05, Table 4).

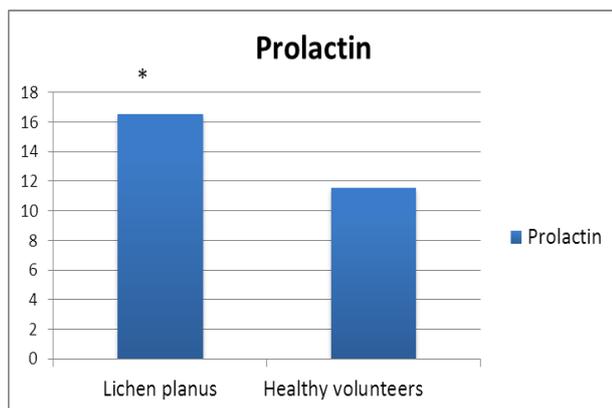
**Table 3: Serum prolactin level in different forms of LP (Mean  $\pm$  SD).**

Parameters	Mucocutaneous LP (n = 11)	Oral LP(n=3)	Cutaneous LP (n = 16)	P value
Prolactin(ng/ml)	18.92 $\pm$ 9.54	14.88 $\pm$ 8.70	15.18 $\pm$ 6.04	0.015*

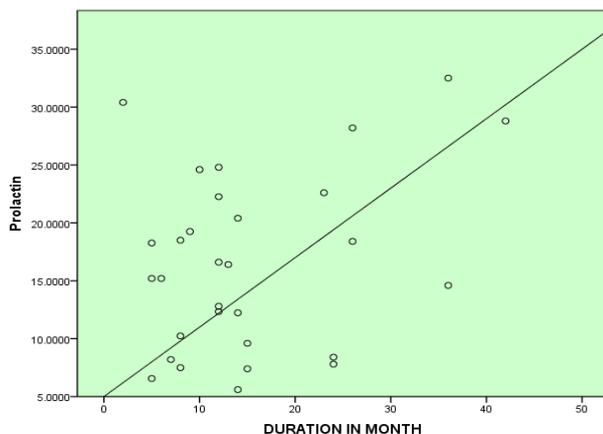
\* means statistically significant with p value < 0.05.

**Table 4: Serum prolactin level in relation to BMI (Mean  $\pm$  SD).**

Parameters	BMI $\geq$ 25	BMI<25	P value
Prolactin(ng/ml)	14.67 $\pm$ 7.28	13.12 $\pm$ 6.29	0.394

**Figure 1: Serum prolactin level (ng/ml) in two groups.**

\* means statistically significant with p value < 0.05.

**Figure 2: Scatter plot showing correlation between prolactin(ng/ml) and duration of illness of lichen planus in months.**

## DISCUSSIONS

In this prospective case control study we aimed to study serum prolactin in LP patients and to compare it with healthy volunteers. There are no literatures on prolactin level in lichen planus to the best of our knowledge.

We found significantly higher prolactin level in lichen planus patients compared to healthy control. We also found higher level of prolactin in mucocutaneous form of illness compared to other type. Prolactin level also showed a positive correlation with duration of lichen planus.

PRL has multiple immune-stimulatory effects and promotes autoimmunity. It increases the synthesis of IFN-gamma, IL-2 and auto antibody by modulating Th1 and Th2 lymphocytes respectively.<sup>[5]</sup> PRL are associated with several autoimmune disease such as SLE, RA, Reiter's syndrome and psoriasis.<sup>[4]</sup>

Prolactin has a proliferative effect on human keratinocytes in vitro and may play a key role in the pathogenesis of psoriasis.<sup>[6,7]</sup> The etiopathogenesis of lichen planus is still unclear. It is also autoimmune in nature and various cytokines involved in its pathogenesis similar to psoriasis.

Several studies had proved association of prolactin with psoriasis.<sup>[8-12]</sup> Some of the studies also found a positive correlation between prolactin level and severity of psoriasis.<sup>[8-11,13]</sup> In contrast few investigators could not find any association between prolactin level and severity of psoriasis.<sup>[14,15]</sup>

However, there are very limited literatures regarding relation of PRL with other dermatological disease like alopecia areata and vitiligo. Gönül et al did not find any association PRL level with vitiligo and concluded that PRL does not play a role in the pathogenesis of vitiligo.<sup>[16]</sup> However, recently in another study serum PRL levels in patients with vitiligo were found to be significantly higher than those of the control subjects. But there were no significant association of PRL level with disease activity or durations.<sup>[11]</sup>

Similarly, Gönül et al also showed no higher serum PRL in patients with alopecia areata compared to control groups and they proved no role of prolactin in the pathogenesis of alopecia areata.<sup>[17]</sup> Although, in a recent study, investigators found significantly higher serum PRL level in patients with alopecia areata than that of the control subjects. In addition they also reported a significant correlation among the type of alopecia and disease activity and the serum PRL.<sup>[11]</sup>

However, we had some limitations in our study. We included small number of patients i.e. 30 in each group. Prolactin level has wide normal reference range and several other unknown factors not mentioned in our exclusion criteria might affect the results in our small study population.

**CONCLUSION**

Hyperprolactinemia is associated with Lichen planus. Prolactin may play a role in the pathogenesis of lichen planus. It may serve as a biological marker of disease activity in patients with lichen planus. Further large scale studies are needed to prove our findings.

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