SERUM PROLACTINE LEVEL IN PATIENTS OF PSORIASIS VULGARIS AND ITS CORRELATION WITH DISEASE SEVERITY: A CASE-CONTROL STUDY

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**Abstract**

**Background:** Psoriasis is an autoimmune chronic inflammatory disorder affecting the skin mediated by T-lymphocytes resulting in production of cytokines which cause hyperproliferation of keratinocytes. Several factors and hormones like Prolactin have an action similar to these cytokines in promoting the multiplication of keratinocytes and other cells like lymphocytes and epithelial cells may have a role on the etiopathogenesis of psoriasis.

**Aim:** The aim of study is to compare the serum Prolactin levels in patients of psoriasis with a control group.

**Setting and study design:** This is a case-control study conducted in the department of Dermatology, Venereology and Leprology GMC, Kota over a period of 1 year from July 2017 to June 2018

**Material and method:** The study included 100 cases of psoriasis (60 males and 40 females) and 100 controls similar for age and sex. Serum Prolactin levels were measured by ECLIA and results were obtained.

**Statistical analysis:** Mean and standard deviation were calculated for each variable. Statistical significance of the results was analyzed using correlation analysis (Pearson correlation coefficient) and independent samples t-test. Statistical significance was assumed at p value < 0.05.

**Result:** Serum Prolactin level was significantly higher in cases of psoriasis compared to controls (p-value < 0.001). PASI score and serum Prolactin levels were found to have a positive correlation (r value = 0.337; p-value: 0.001). No significant correlation was found between serum levels of Prolactin and duration of disease r value = -0.034, P value = 0.733. Serum Prolactin level was higher in male patients compared to females patients.

**Conclusion:** High serum Prolactin may be a biological marker of disease severity in psoriasis and may have a role in the pathogenesis of psoriasis. Further studies with large sample size are required to confirm this hypothesis.

**Introduction**

Psoriasis is a T-cell mediated chronic autoimmune disease characterized by proliferation of keratinocytes and accumulation of T cells in the epidermis and dermis of psoriatic lesions. \([1] [2]\)

It is influenced by multifactorial etiologies like genetic, environmental, hormonal factors and psychoemotional stress. \([3,4]\)

Severity of psoriasis may be influenced by the level of hormones. Disease frequency is greater during puberty \([5]\) and menopause \([6]\). Similar peaks are seen around the age of 30 and 50 years thus highlighting a possible role of hormones by altering the factors involved in its evolution.

Prolactin (PRL) is an anterior pituitary polypeptide hormone. It forms a “prolactin-circuit” between the central nervous system and the skin \([8,9]\) acting as a neuroendocrine modulator of skin epithelial cell proliferation and plays a significant role in osmoregulation of epithelial tissue and has immunoregulatory properties.

Few studies have reported an increase in serum PRL levels in psoriasis patient and in presence of prolactinoma, exacerbation of psoriasis has been reported.
There is a lacuna of data available in the literature regarding the role of Prolactin in the etiopathogenesis of psoriasis. The present study was aimed to evaluate the Prolactin in pathogenesis of psoriasis.

MATERIAL AND METHODS

This study was an institution based case-control study conducted in the Department of Dermatology, Venereology and Leprosy in Govt. Medical College Kota over a period of 1 year from July 2017 to June 2018.

Our study included 100 patients with chronic plaque psoriasis who had no topical and systemic treatment for the last 4 weeks at attending OPD comprised 60 males and 40 females with a mean age of 37.98 years.

The control group comprised 100 healthy volunteers, similar for age and sex (60male; 40female), with a mean age of 37.75 years. The controls had no history of any skin abnormalities or any chronic debilitating disease. Other demographic variables should be matched in both group

Diagnosis of psoriasis was based on clinical findings and history of the disease.

A complete dermatological examination was done for each patient to determine the extent of and distribution of disease. At the time of attending the skin outdoor patient department, PASI and body surface area were calculated. The PASI is the current gold standard for assessing the clinical severity and extent of psoriasis. The score is obtained by grading three variables (erythema, infiltration and desquamation) from 0 to 4, weighted by the area of involvement. Each body region is weighted according to its approximate percentage of the whole body, based on the "rule of nines". The final score ranges from 0 to 72. Scores <3 represent mild, ≤10 moderate and > 10 severe cases of psoriasis.

Exclusion criteria were pregnancy, breastfeeding, and evidence of renal, hepatic, endocrinopathy (Prolactinoma, Hypothyroidism) or psychiatric disease. Patients who were receiving any medications affecting PRL such as phenothiazines (chrompromazine), antidopaminergic agents (metaclopromide), antihypertensive agents (calcium channel blockers, methyldopa) and H2 blockers (cimetidine) were also excluded from the study with an aim to avoid instances of secondary hyperprolactinaemia.

Informed written consent was obtained from all the participants included.

Blood samples were taken in the morning between 8.00 and 10.00 A.M in both patients and controls in regard to the circadian variation of PRL secretion. In women, measurements were taken in the premenstrual phase of the cycle.

Levels of PRL were quantitatively estimated using immunoassay (ECLIA). Reference range for PRL was 2-18 ng/ml for males and 2-29 ng/ml for females measured by ECLIA.

Statistical analysis

The statistical analysis was carried out using Statistical Package for Social Sciences. The mean and standard deviation were determined for each variable. All the results were expressed as mean±S.D.Comparisons of data was done by applying student t-test. The correlation between severity of disease and prolactin levels were determined by pearson’s correlation co-efficient. p-value <0.05 was considered significant.

RESULT

The present study comprised 100 patients of psoriasis and 100 controls. Out of 100 cases; 60(60%) were male and 40(40% ) were female with male and female ratio of 1.50:1 while in control group 61(61%) male and (39%) female with male female ratio was 1.56:1.

Patients of psoriasis were in age group from 16 years to75years. (Mean37.98 ± 13.93).The controls were in the age group from 19 to 76years (Mean 37.75±14.98).

There was no significant difference between the age and sex of two groups.

In case group body surface area involved by psoriasis was between 7 to 60% [Mean25.39±14.07]. Amongst 100 cases, 13[13%] had ≤10% of body surface area involved while 87[87%] had involvement of >10% of BSA.[ Figure-1 ].

According to PASI score, patients were classified into mild, moderate and severe psoriasis. There were 1(1%) mild, 58(58%) moderate and 41(41%) severe cases in the study. [Figure -2]PASI score ranged from
2.6 to 35.4 with a mean of 12.42±7.82. Significant correlation was seen between PASI and serum Prolactin levels (r =0.337, p value= 0.001). [Figure-3]

In our study, 58% patient had disease for less than 5 years while 42% patient had disease for more than 5 yrs. [Figure-4] The duration of disease activity was found from 1 to 25 years with mean duration of disease 6.24±4.81. In our study, there was no significant correlation between duration of psoriasis and serum Prolactin level (r value = -0.034, P value =0.733). [Figure-5]

In our study, Serum Prolactin level ranged from 1.40 to 59.54ng/ml with a mean value of 13.64±8.53ng/ml in case group while in control group, the values ranged from 3.99 to 18.06ng/ml with a mean value of 9.65 ±3.99ng/ml. Serum Prolactin levels in case group was higher as compared to control group with significant difference between cases and controls (p value <0.001). [Figure-6]

In our study out of 100; 14 (14%) cases had high serum Prolactin which include 13(13%) male patients and 1(1%) female patient. [Figure-7]

In our study Serum Prolactin level was higher in male patients with mean 13.42±9.43 as compared to male patients in control group with mean 8.89±3.87. It was statistically significant with (P value 0.0007).

In our study Serum Prolactin level was higher in female patients with mean 13.97 ±7.08 as compared to female patients in control group with 10.84 ± 3.94. It was statistically significant with (P value-0.0179)
Figure 6: Comparison of mean serum Prolactin levels in cases and controls

Figure 7: Association between serum Prolactin levels in cases and controls

### Table 1: Statistical Parameters of Duration of Psoriasis, BSA and PASI

<table>
<thead>
<tr>
<th></th>
<th>Duration of Psoriasis in Years</th>
<th>BSA Involved (%)</th>
<th>PASI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>6.24</td>
<td>25.39</td>
<td>12.42</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>4.81</td>
<td>14.07</td>
<td>7.82</td>
</tr>
<tr>
<td>Median</td>
<td>5</td>
<td>20</td>
<td>9.45</td>
</tr>
<tr>
<td>Minimum</td>
<td>1</td>
<td>7</td>
<td>2.6</td>
</tr>
<tr>
<td>Maximum</td>
<td>25</td>
<td>60</td>
<td>35.4</td>
</tr>
</tbody>
</table>

### Table 2: Comparison of Mean Serum Prolactin Levels in Case and Control

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>13.64</td>
<td>8.53</td>
<td>11.86</td>
<td>1.40</td>
<td>59.54</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Control</td>
<td>9.65</td>
<td>3.99</td>
<td>9.75</td>
<td>2.80</td>
<td>18.06</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3: Association Between Serum Prolactin Levels and Psoriasis Cases and Controls

<table>
<thead>
<tr>
<th>Serum Prolactin Levels</th>
<th>Case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Normal</td>
<td>85</td>
<td>85.00%</td>
</tr>
<tr>
<td>Hypo</td>
<td>1</td>
<td>1.00%</td>
</tr>
<tr>
<td>Hyper</td>
<td>14</td>
<td>14.00%</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

Chi-square = 16.216 with 2 degrees of freedom; p value <0.05.

### Table 4: Association Between Serum Prolactin Levels and Gender in Cases and Controls

<table>
<thead>
<tr>
<th>Serum Prolactin Levels</th>
<th>Cases</th>
<th>Controls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Hyper</td>
<td>1</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Hypo</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Normal</td>
<td>39</td>
<td>46</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>60</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td>121</td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.017</td>
<td>0.026</td>
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</tbody>
</table>
TABLE 5: COMPARISON OF MEAN SERUM PROLACTIN LEVELS ACCORDING TO GENDER IN CASE AND CONTROL GROUP

<table>
<thead>
<tr>
<th>Gender</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Median</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Case</td>
<td>60</td>
<td>13.42</td>
<td>9.43</td>
<td>11.98</td>
<td>0.0007</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>61</td>
<td>8.89</td>
<td>3.87</td>
<td>8.80</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>Case</td>
<td>40</td>
<td>13.97</td>
<td>7.08</td>
<td>11.79</td>
<td>0.0179</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>39</td>
<td>10.84</td>
<td>3.94</td>
<td>10.90</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 6: Correlation of serum Prolactin levels with Duration of disease, BSA and PASI

<table>
<thead>
<tr>
<th>Serum Prolactin Levels</th>
<th>N</th>
<th>Pearson Correlation (r)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of psoriasis</td>
<td>100</td>
<td>-0.034</td>
<td>0.733</td>
</tr>
<tr>
<td>BSA involved (%)</td>
<td>100</td>
<td>0.276</td>
<td>0.005</td>
</tr>
<tr>
<td>PASI</td>
<td>100</td>
<td>0.337</td>
<td>0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

Exact etiology of psoriasis was not clear. It has been reported stress and hormonal factors to be implicated in the pathogenesis of psoriasis. [10]

Despite that role of PRL in psoriasis vulgaris pathogenesis is still unclear, its role in development of autoimmune diseases has become accepted [11]

It has been hypothesized that PRL may modulate the skin immune system and may be involved in the pathogenesis of psoriasis. Prolactin appears to play a role in the activity of autoimmune disorders such as systemic lupus erythematosus and rheumatoid arthritis. It influence both humoral and cell mediated immune reactions, and an important role in the expression of autoimmune diseases.[12] It has been reported that stress trigger and exacerbate psoriasis; make a link between prolactin and the disease pathogenesis.[13]

Prolactin is a versatile polypeptide hormone secreted mainly by the lactotrophic cells of pituitary gland and partially by some immune cells [14]. It influences differentiation and maturation of T and B lymphocytes via its receptor and their precursors (e.g. thymocytes, B lymphocytes) and is one of the factors supporting their autoreactivity [15]. Binding to specific skin receptors, modulation of cytokine release in the skin, and stimulation of somatomedin release by mesenchymal cells are among the suggested pathways by which prolactin could affect epithelial cell growth in the skin

Prolactin facilitate the psoriatic plaque formation by the infiltration of type 1 T- helper cells into psoriatic lesions and by inhibition of T- suppressor cell by increasing IFNγ induced transcription and secretion of chemokines (CXCL9, CXCL10, CXCL11). It also stimulates keratinocyte hyperproliferation by production of IFNγ from T lymphocyte and increase VEGF production that promotes angiogenesis which are the hallmark features of psoriasis. [16,17,18,19]

A study by Weber et al first claimed that bromocriptine, a potent dopaminergic inhibitor of pituitary Prolactin secretion induced remission of psoriatic cutaneous lesions and even psoriatic arthritis.[20] Similar results on the role of prolactin in pathogenesis of psoriasis was found by Paus R et al in his study. [21]

Eulry et al postulated that retinoids also produce antipsoriatic effect by decreasing Prolactin secretion from pituitary gland [22] Psoriasis tend to be stable during pregnancy and worsen during early postpartum period due to physiological hyperprolactinemia associated with lactation.

In present study serum Prolactin level was examined in 100 patients of psoriasis and 100 controls. In our study, serum Prolactin level was higher in patients compared to control group and difference was significant (P value <0.001). There is also significant correlation between PASI and serum Prolactin level.

The result of the study was quite similar to the findings in the study of Giasuddin et al. which revealed that serum PRL levels were increased in psoriatic patients as compared to controls. [23] This suggested that raised serum PRL level may have a role in the hyperproliferation of keratinocytes in vivo, the hallmark of the psoriasis disease process.
The result of our study was consistent with the result obtained by Dilme careass et al in her study of 20 patients and 20 controls. They observed significant increase in serum Prolactin in the psoriasis group before treatment with tacalcitio (21.4 ±16.7 ng/ml) as compared to control group ( 8.4 ± 5.2 ng/ml) (P<0.001). There was significant positive correlation found between pretreatment serum Prolan level and PASI. There was significant decrease serum Prolactin level in level after tacalcitio treatment.[24]

Our result was also similar to that obtained in the study by Mohammad ab et al. which included 60 patients of psoriasis and 60 healthy controls. Serum level of PRL was significantly higher in psoriatic patients than control (P < 0.05). There was positive correlation between serum PRL levels and PASI score. Also, serum PRL levels were found to be reduced after treatment although the difference was statistically insignificant.[25]

Madhur et al. also observed serum Prolactin levels higher in the study group (65.40 ± 21.99 ng/ml) as compared to control group (12.758 ± 4.65 ng/ml) (p<0.001). Significant positive correlation is found between serum Prolactin level and PASI.[26]

In a study by El-Khateeb et al. that included 15 psoriasis patients and 15 controls, PASI score was evaluated, and PRL levels in serum and blister fluid were assessed. They found that PRL levels were significantly elevated in blister fluid of psoriatic lesonal skin. They also noted a positive correlation of serum PRL level between lesonal and nonlesional skin in psoriasis and between serum and clinically normal skin in both psoriasis and control subjects.[27]

Our study was similar to the study of Abtel sh. et al. which included 100 psoriasis patients and 100 controls. Serum Prolactin level was significantly higher in patient group than control group <0.05. Thus, there was a positive correlation between PRL levels and the severity of psoriasis (P value< 0.05). Also, elevated mean Prolactin level among female patients was higher than male patients and serum Prolactin levels were higher in severe cases of psoriasis than in mild and moderate cases.[28]

Husakova et al. in 2015 demonstrated correlation between increased PRL serum levels and psoriatic arthritis, therefore elevated PRL serum levels might represent a marker of inflammatory joint disease in patients suffering from psoriasis vulgaris [29].

Study by Hedman et al. measured the levels of PRL and other hormones in blood and synovial fluid in patients with arthritis of the knee associated with psoriasis (seven cases), and reported that there were no significant differences between patient and control groups.[30]

In a study of 35 patients of psoriatic arthritis who were treated with bromocriptine in a dosage 2.5 mg titrated up to 30 mg/day, significant improvements were seen in patients who were resistant to conventional therapy.[31]

In 2000, Sánchez Regaña and Umbert Millet reported that bromocriptine induce remission in psoriatic lesion in three patients of psoriasis with associated prolactinoma. [32]

In a study by Hau C S et al. topical application of imiquimod on back skin of mice PRL enhances inflammation and Th1 and Th17 cytokine production induced psoriasisform skin changes.[33]

Azizzadeh et al. observed no significant difference in mean serum prolactin levels between patients and controls. However, serum prolactin levels varied with severity of disease in patients .[34]

Priestley et al. in their study did not find any significant difference in PRL and growth hormone levels between patients and controls.[35]

In our study, we found correlation between serum PRL levels and psoriasis. Our study also revealed correlation between PRL levels and the severity of disease. On the basis of our study results, the role of PRL in the pathogenesis of psoriasis cannot be ruled out. Small number of patients/controls and no therapeutic follow up were major limitation of our study.

Additional studies with larger sample size and including patients with severe psoriasis are needed in order to confirm our hypothesis and validate our findings.

**CONCLUSION**

On comparison of result of present study with the other studies mentioned, it can be concluded that the high serum PRL levels are biological markers of disease severity. Further, studies with large sample size are required to confirm whether PRL plays a part in the etiopathogenesis of psoriasis. Prolactin may be novel therapeutic target in psoriasis and other skin disease that worsen in response of...
psychological stress. In well designed studies, Bromocriptine was found to be a useful therapeutic option and should be recommended in severe case of psoriasis even if prolactin levels are normal. Lastly, further studies should also be done in future to develop more specific therapy using antibodies against PRL.

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30. Hedman M, Nilsson E, de la Torre B. Low blood and synovial fluid levels of sulphonyl conjugated steroids in rheumatoid arthritis. Clin Exp Rheumatol. 1


