# RESEARCH ARTICLE

## SERUM LEVELS OF SE-SELECTIN, TNF-α AND IL-1β IN PATIENTS OF PSORIASIS BEFORE AND AFTER TOPICAL THERAPY IN PATIENTS OF PSORIASIS

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## ABSTRACT

**Background:** Psoriasis is a T-cell mediated immunological disorder with numerous cytokines and adhesion molecules at play in its pathogenesis. Role of TNF-α, IL-1β and E-selectin has been studied by a few authors. But the studies are very limited in number. We plan to study these markers before and after topical therapy in patients of Psoriasis.

**Aims and Objectives:** To study the serum levels of sE-selectin, TNF-α and IL-1β in patients of psoriasis and compare them with controls, Psoriasis Severity index and with each other.

**Material and Method:** A prospective study of patients presenting with newly diagnosed Psoriasis at Dermatology OPD of Smt. Sucheta Kriplani Hospital, New Delhi. Follow-up was done after topical therapy with Coal tar, Salicylic acid and Dithranol. A total of 6 patients could be followed up. Serum samples were taken for ELISA determinations of TNF-α, IL-1β and sE-selectin at diagnosis and at 6 months follow-up visit.

**Results:** In the present study the cases ranged from 8 to 50 years. Four patients had psoriasis vulgaris, 1 had Palmoplantar psoriasis and one had Pustular psoriasis. PASI Score ranged from 1.6 to 8.8. sE-selectin level in cases was $177.4 \pm 81.21$ ng/ml and reduced after therapy to $101.17 \pm 34.64$ ng/ml ($p = .092$). TNF-α level in cases was $32.05 \pm 42.27$ pg/ml and reduced after therapy to $14.31 \pm 15.25$ pg/ml ($p = .201$). IL-1β levels in cases was $20.78 \pm 18.80$ pg/ml and after therapy the levels reduced to $9.13 \pm 5.74$ ($p = .210$).

**Conclusion:** sE-selectin, TNF-α and IL-1β levels are increased in patients with psoriasis vulgaris as compared to controls. After therapy the levels reduce from the initial value but not enough to reach a statistical significance and remain higher than controls. This shows that these markers play an integral role in the pathogenesis and can be essential targets in formulation of newer therapies. Further studies as required to advance our knowledge in possible newer treatments for Psoriasis.

## INTRODUCTION

Psoriasis is an immunological disorder with skin lesions as the main presenting feature. The most common form of psoriasis is psoriasis vulgaris, which is characterized by sharply demarcated, red, and scaly symmetrical plaques on the elbows, knees or scalp. Psoriasis is not just limited to skin but further can cause psoriatic arthritis. (Taylor *et al.*, 2006) In severe cases, psoriatic arthritis can be disabling and cause irreversible damage to joints. Athough a variety of treatment options are available majority of patients have expressed dissatisfaction from the treatment quoted as high as 83% by some surveys. (Today, 2017) Psoriasis is graded using Psoriasis Area and Severity Index (PASI) and is categorized into mild, moderate and severe based on PASI score. (Schmitt and Wozel, 2005) Hence, further insights into the immunological mechanism of psoriasis are required to provide immunotherapy in such cases. Increase in the levels of TNF-α in psoriatic individuals is already known and TNF-α antagonists are being used in psoriasis treatment. (Mussi *et al.*, 1997; Jacob *et al.*, 2003; Gottlieb *et al.*, 2003) There are a few studies that show sE-selectin levels to be increased in psoriasis patients. But Indian literature is very limited in this aspect. (Czech *et al.*, 1996; Borská *et al.*, 2006; Long *et al.*, 2010) We plan to study the serum levels of sE-selectin and two activators of E-selectin i.e TNF-α AND IL-1β and correlate them with each other in patients of Psoriasis.

**Aims and Objectives**

1. To study the serum levels of sE-selectin, TNF-α and IL-1β in patients of psoriasis and compare them with controls.
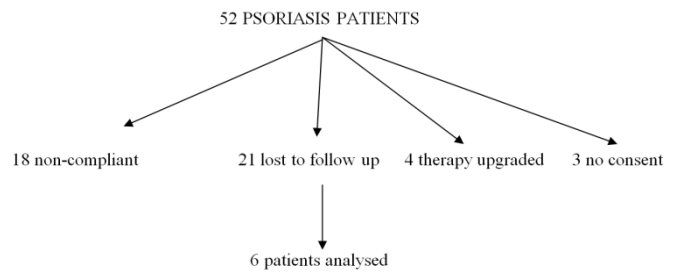
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2. To study changes in the levels of sE-selectin, TNF-α and IL-1β in patients after therapy.
3. To correlate the levels of sE-selectin, TNF-α and IL-1β with each other and with PASI.

## MATERIALS AND METHODS

Psoriasis patients attending the dermatology OPD of our institute were screened and only the first time patients who had not taken any treatment were included in the study. A signed informed consent was taken from all before proceeding to the study. They were scored using PASI. Venous blood sample for serum measurement of sE-selectin, TNF-α and IL-1β was taken followed by skin biopsy for confirmation of diagnosis of Psoriasis. sE-selectin, TNF-α and IL-1β were measured by ELISA kit method (Diaclone, France). The patients were given topical treatment i.e coal tar(6%) +dithranol + salicylic acid (3%). The patients were followed up every 3 weeks. At the 6 month visit repeat PASI score assessment was done and repeat serum sample was taken for of sE-selectin, TNF-α and IL-1β levels. Healthy volunteers with no family history of psoriasis were also included as controls for the serum samples. A total of 52 patients were included in the study, out of which 21 were lost to follow-up, 18 patients had a history of irregular/non-compliance to treatment, 4 needed to be upgraded to Psoralen Ultra Violet A (PUVA) therapy/oral therapy and 3 did not give consent for further testing. Hence, blood samples of only 6 patients could be analysed at the follow-up visit.

52 PSORIASIS PATIENTS

18 non-compliant     21 lost to follow up     4 therapy upgraded     3 no consent

6 patients analysed

## RESULTS

On analysis of 6 cases of Psoriasis Vulgaris and 6 controls the age ranged from 8 to 50 years in cases (mean 34.67± 14.61) and 19 to 40 years in controls (mean 30.5±10.13). The cases had 3 males and 3 females where as controls had 4 males and 2 females. Of the 6 patients 4 had psoriasis vulgaris, 1 had Palmoplantar psoriasis and one had Pustular psoriasis. Histopathology was available in all the cases and diagnosis was confirmed. Legs were the most common site of involvement with arms next in line and palms as the least common site affected. (Fig 1,2)  Duration of Psoriasis varied from 2 months to 3 yrs with one patient having the lesions since 20 years. PASI Score ranged from 1.6 to 8.8 with a mean of 3.75±2.97. 5 patients had mild psoriasis (<7) and 1 had moderate psoriasis (>=7). Post therapy PASI score reduced and ranged from 1.1 to 5.7 with a mean of 2.76±1.56. (p=0.200). (Table 1) sE-selectin level in cases was 177.4±81.21ng/ml as

### Table 1. PASI Score before and after therapy

| Case no. | PASI | PASI ( pt) | p-value |
|---|---|---|---|
| 1 | 1.8 | 2.3 | .200 |
| 2 | 1.6 | 1.1 | |
| 3 | 1.8 | 2 | |
| 4 | 2.5 | 2.5 | |
| 5 | 6 | 3 | |
| 6 | 8.8 | 5.7 | |

### Table 2. TNF-α, sE-selectin and IL-1β levels in cases and controls

| Case No. | TNF-α (pg/ml) | | p-value | sE-SELECTIN (ng/ml) | | p-value | IL-1β (pg/ml) | | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | Case | Control | | Case | Control | | Case | Control | |
| 1 | 3.23 | 10 | .240 | 144.75 | 15 | .024 | 6.9 | 6.8 | .148 |
| 2 | 5.32 | 8.4 | | 112.1 | 29 | | 7 | 7.2 | |
| 3 | 6.69 | 8 | | 182.52 | 62.5 | | 12 | 9.1 | |
| 4 | 19.2 | 10 | | 108.99 | 107.5 | | 15.6 | 8 | |
| 5 | 45.87 | 9 | | 187.5 | 8 | | 27.2 | 8.4 | |
| 6 | 112 | 9.7 | | 328.54 | 27 | | 56 | 10.3 | |

### Table 3. TNF-α, sE-selectin and IL-1β levels before and after therapy

| CASE NO. | TNF-α | | p-value | sE-SELECTIN | | p-value | IL-1β | | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | Before | After | | Before | After | | Before | After | |
| 1 | 3.23 | 8.06 | .201 | 144.75 | 110 | .092 | 6.9 | 11 | .210 |
| 2 | 5.32 | 11 | | 112.1 | 121 | | 7 | 6.5 | |
| 3 | 6.69 | 5.32 | | 182.52 | 120 | | 12 | 2 | |
| 4 | 19.2 | 11.2 | | 108.99 | 116 | | 15.6 | 14 | |
| 5 | 45.87 | 5.3 | | 187.5 | 45 | | 27.2 | 16.8 | |
| MEAN | 112 | 45 | | 328.54 | 149 | | 56 | 4.5 | |

### Table 4. Correlation of levels TNF-α, sE-selectin and IL-1β in cases

| | sE-selectin | TNF-α | IL-1β |
|---|---|---|---|
| sE-selectin | | .011 | .009 |
| TNF-α | .011 | | .000 |
| IL-1β | .009 | .000 | |

compared to 41.5±37.38ng/ml in controls. The difference in levels was statistically significant (p=.024). The levels of sE-selectin reduced after therapy to 101.17±34.64ng/ml but the reduction was not statistically significant (p=.092) TNF-α level in cases ranged 3.23 pg/ml to 112.0 pg/ml (mean 32.05±42.27 pg/ml) whereas in controls it ranged from 8.0pg/ml to 10.0 pg/ml (mean 9.18±0.85pg/ml). The difference was not statistically significant (p=.240). After therapy the TNF-α levels reduced to 14.31±15.25pg/ml and the reduction could not reach statistical significance (p=.201) IL-1β levels in cases was 20.78 ±18.80 pg/ml as compared to 8.30±1.28 pg/ml in controls (p=0.148). After therapy the levels reduced to 9.13±5.74 (p=.210). (Table 2) The levels of sE-selectin, TNF-α and IL-1β correlated with each other and also with PASI (Table 3).
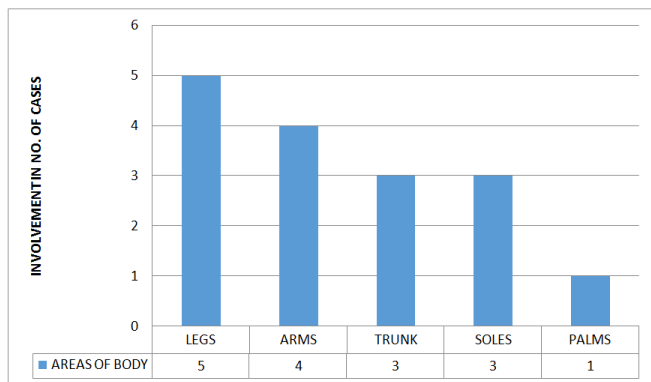


**Figure 1. Frequency of involvement of different parts of body**



**Figure 2. Psoriasis Patch. Trunk involvement**

## DISCUSSION

6 of 52 patients could be followed up after 6 months of topical therapy with salicylic acid and coal tar. The patients in the present showed a reduction in PASI, although none had complete clearance of lesions. The reduction the PASI score was not statistically significant (p=.200) post-therapy. We postulate that this could have been due to requirement of alternative therapy by the patient. Borska *et al* reported a significant (p<.001) reduction in PASI after Goekerman's therapy (crude coal tar and UV radiation). The mean PASI score before treatment was 22.2±6.9 and it reduced to 6.3±3.7 after therapy. (Borská *et al*., 2006) Long *et al* also studied the effect of therapy (narrow band UV-B) on psoriasis patients. He

reported a significant reduction (p<.001) in PASI values of patients after UV-B therapy (mean PASI 6.02±2.07) as opposed to pretreatment values (mean PASI 23.70±10.14). (Long *et al*., 2010) Czech *et al* also reported a significant decrease (p<.05) in PASI score of cases after treatment with dithranol and petrolatum for 2-4 weeks. (Czech *et al*., 1996) In our study there was a reduction in the mean serum sE-selectin levels from 177.40 ng/ml to 101.17 ng/ml after therapy, but this decline could also not reach statistical significance (p=.092).When compared to mean control sE-selectin levels (41.5ng/ml) the post therapy levels remained significantly high (p=.010). Similar findings were reported by Czech *et al* where patients were treated by dithranol and petrolatum for 2-4 weeks. They did not find any significant change in sE-selectin levels after therapy. (Czech *et al*., 1996) In study by Krasowaska *et al* topical therapy (dithranol) was given to the both acute (<2 months duration) and chronic cases (>2 months duration) for 4-8 weeks. After treatment, there was no significant reduction in levels. When compared to controls, the levels were still significantly raised in both acute and chronic cases (p<.001 and p<.009 respectively). (Krasowska *et al*., 1999) Similarly Kowalzick *et al* did not report any significant decrease in sE-selectin levels after dithranol and UV-B therapy for 22.8±11.2 days. (Kowalzick *et al*., 1994) On the Contrary, Borska *et al* reported significant decrease (p<.05) in sE-selectin levels from 91.03±59.85 ng/ml to 85.36±49.83ng/ml after 8 to 30 days (average 17 days) of Goekerman's therapy (crude coal tar and UV radiation). Long *et al* also studied serum sE-selectin levels after UB-B phototherapy. The serum sE-selectin levels reduced from 88.82±19.72ng/ml to 79.96±17.50ng/ml. This decrease was statistically significant (p=0.000) as compared to pretreatment levels. (Long *et al*., 2010)

There was also a reduction in the serum TNF-α levels from 32.05 pg/ml to 14.31 pg/ml, but this decline in levels was not statistically significant (=.201 pg/ml). On comparing the post therapy levels with mean control levels (9.18pg/ml), the levels were not statistically significant (p=.440). Similarly Borska *et al* did not find any significant decrease in the levels of TNF-α after treatment with Goekerman's therapy (before treatment – 1.68±0.83 pg/ml, after treatment – 1.51±0.72 pg/ml). (Borská *et al*., 2006) In the study by Tiagalnova *et al* patients were provided with Acitretin, Cyclosporin and Goekerman therapy. They did not report any significant change in the level of TNF-α following treatment. (Tigalonova *et al*., 1994) However, Chodorowska *et al* reported significant decrease (p<0.02) in mean serum levels of TNF-α in psoriasis patients following topical treatment with dithranol, duration of treatment being 21-68 days. The post treatment levels (11.48±6.83pg/ml) observed by them were even significantly lower than (p<0.02) control levels (17.7±7.77pg/ml). (Chodorowska, 1998) Similarly Mussi *et al* reported a significant reduction in TNF-α levels after treatment. IL-1β levels also reduced from 20.78 pg/ml to 9.13pg/ml (p=.210). When the mean levels were compared with those of controls (8.30pg/ml) there was no significant difference (p=.148). To the best of our knowledge there are no studies in serum that compare the effect of therapy on levels of serum IL-1β in psoriasis patients.

## DISCUSSION

sE-selectin, TNF-α and IL-1β play an important role in pathogenesis of Psoriasis, correlate with Psoriasis severity and with each other. They show a reduction after topical therapy

but not enough to reach a statistical significance. However, the present study is limited by the number of cases. Larger scale studies are required to validate the role of these serum markers and formulation of newer treatment modalities. Since most of the patients are not able to reach complete remission and have a high rate of morbidity, alternate therapy is required and further research is needed for the same.

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