

Plasma-soluble urokinase plasminogen activator receptor (suPAR) levels in psoriasis patients and correlation with disease severity

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Abstract

Objective: Psoriasis is a chronic, relapsing, inflammatory, hyper-proliferative skin disease. Plasma-soluble urokinase plasminogen activator receptor (suPAR) is released from the cell membrane-bound plasminogen activator and is a new biomarker of systemic inflammation. The aim of this study is to investigate plasma levels in psoriasis patients and determine their correlation with the Psoriasis Area and Severity Index (PASI) score.

Materials and methods: The plasma suPAR levels of 50 healthy individuals and 65 psoriasis patients were measured using the Micro-ELISA method and the relation with PASI was investigated.

Results: On comparing plasma suPAR levels of the psoriasis patients with the control group consisting of healthy individuals, no statistically significant difference was determined (5.29 ng/ml \pm 2.12 and 6.03 ng/ml \pm 2.42, respectively, $p = 0.326$; Table 1). Likewise, there was no significant correlation between the suPAR levels and PASI score ($r = 0.147$, $p = 0.243 > 0.05$).

Conclusions: There was no statistically significant difference in the plasma SuPAR levels of psoriasis patients compared to the control group. Nevertheless, we firmly believe that plasma SuPAR, a new biomarker, could indicate disease severity if conducted with larger patient series and with moderate to severe psoriasis patients.

Keywords: psoriasis, suPAR, PASI

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Introduction

Psoriasis is a hereditary polygenic chronic and recurrent inflammatory skin disease with a multifactorial etiology. The disease, with a genetic predisposition, is considered to emerge due to the impact of infections and environmental factors such as emotional stress and trauma with T-cell-mediated immune mechanisms (1–3). Currently there is no laboratory indicator indicating disease activity and making possible the comparison of treatment modalities in psoriasis.

Soluble urokinase plasminogen activator receptor (suPAR) is a glycosylphosphatidylinositol (GPI) membrane protein bound to a urokinase-type plasminogen activator receptor (uPAR) in soluble form. An increase in immune system activation will lead to elevated serum suPAR levels (4). In recent years, it has been defined as a valuable indicator of immune system activation. Elevated suPAR levels have been widely demonstrated in several studies on inflammatory diseases and cancer (5–8).

The aim of this study is to analyze plasma suPAR levels of psoriasis patients and determine whether there is a possible relation to disease intensity.

Materials and methods

The participants in this study were 65 patients diagnosed with clinical and histopathological psoriasis, 35 (53%) female and 30 male (46.2%), and 50 healthy individuals (25 female and 25 male).

Subsequent to Selçuk University Faculty of Medicine Ethics Committee approval, the study was conducted from January 2013 to July 2013. Informed consent was obtained from all participants

in this study. Patients that underwent systemic, topical anti-psoriatic, and/or photo (chemo) therapy within the previous four weeks were excluded from the study. Patients with hypertension, diabetes mellitus, chronic renal failure, liver disease, heart failure, acute or chronic infection, accompanied autoimmune disease, and malignancy were also excluded.

Socio-demographic information for all participants was recorded, and the psoriasis area severity index (PASI) was used to calculate disease severity.

Five ml of venous blood was taken at 8:00 am from the patient and control groups. Peripheral venous blood samples were obtained using EDTA-containing blood collector tubes and plasma samples through centrifuging. Plasma samples were stored deep frozen at -80°C until suPAR levels were measured. suPAR assays were evaluated using a micro ELISA reactive receptor (PLAUR / uPAR) ELISA Kit, Hangzhou East Biopharm Co. Ltd. Hangzhou, PRC and microplate reader (BiotekELx 800, BioTek Instrumentations, Inc., Winooski, VT, USA).

During the statistical analysis, the Mann-Whitney U test was used for two independent groups with normal distribution, and for abnormal distribution Spearman's rho correlation coefficient was used. As a statistical significance threshold, the level $p < 0.05$ was accepted.

Results

Out of the 65 psoriasis patients, 35 (53.8%) were female and 30 (46.2%) male. The control group, 50 in total, consisted of 25 (50.0%) healthy female and 25 (50.0%) healthy male participants. The mean age of the psoriasis patients was 36.17 ± 13.93 years and

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of the control group 33.82 ± 13.16 years. There was no statistically significant difference in terms of age and sex between the groups ($p > 0.05$). In the psoriasis patient group, 42 (64.6%) cases had plaque-type psoriasis and 23 (35.4%) guttate psoriasis. The mean PASI score of the patient group was 11.3 ± 7.8 and mean disease duration 11.1 ± 11.5 years. No statistically significant difference was seen on comparing patient and control-group plasma suPAR levels (5.29 ± 2.12 ng/ml and 6.03 ± 2.41 ng/ml, respectively, $p = 0.326 > 0.05$; Table 1). Likewise, there was no statistically significant correlation between plasma suPAR levels and PASI scores ($r = 0.147$, $p = 0.243 > 0.05$). No statistically significant difference was seen in terms of disease duration (> 10 and < 10 years) and mean suPAR levels ($p = 0.890$; Table 2). In terms of sex in the psoriasis group, there was no statistically significant difference in the suPAR levels ($p = 0.114$; Table 3).

Table 1 | Plasma suPAR levels in psoriasis and control groups.

	suPAR (pg/mL)	P value
Psoriasis	5.29 ± 2.12	0.326
Control	6.03 ± 2.41	

$P > 0.05$

Table 2 | Plasma suPAR levels by mean duration in the psoriasis group.

Psoriasis duration	n	suPAR (ng/mL)	P value
< 10 years	31	5.29 ± 2.36	0.890
> 10 years	34	5.3 ± 2.16	

$P > 0.05$

Table 3 | Plasma suPAR levels by sex.

Sex	n	suPAR (ng/mL)	P value
Female	35	5.75 ± 1.91	0.114
Male	30	4.98 ± 2.26	

Discussion

To the best of our knowledge, this study is the first to investigate suPAR levels in psoriasis patients. Compared to the control group, the plasma suPAR levels of psoriasis patients revealed no statistically significant difference. These outcomes might be attributed to the fact that the psoriasis patients had mild to moderate levels of disease severity in this study.

Urokinase-type plasminogen activator receptor (uPAR) contains three fields and is present in monocytes, activated-T lymphocytes, macrophages, endothelial cells, keratinocytes, fibroblasts, smooth muscle cells, megakaryocytes, and certain tumor cells. suPAR divides itself from membrane-bound uPAR and, depending on the immunity activation, is present in various concentrations in the plasma, urine, blood, and serum fluid (9–11). Hence, increased immune system activation leads to elevated suPAR serum levels. The same has been reported in a variety of pathological conditions, including paroxysmal nocturnal hemoglobinuria, human immunodeficiency virus type-1 (HIV-1) infection, malaria, pneumococcal and streptococcus pneumonia bacteremia, sepsis, bacterial and viral central nerve system (CNS) infection, active tuberculosis (TB), and even various solid tumor forms (12–17).

Many experimental studies have determined increased suPAR

systemic levels in cancer as well as in various infectious and inflammatory diseases. Among the infectious and inflammatory diseases are human immunodeficiency virus (HIV), malaria, tuberculosis, central nervous system infections, urinary tract infections, arthritis, liver fibrosis, and inflammatory bowel disease (18–23).

Systemic levels of suPAR were found to be a strong prognostic value in HIV-infected individuals. In addition, it is of prognostic value in predicting the course and severity of cancer patients (24).

Likewise, quite high systemic suPAR levels have been determined in critical and serious diseases such as sepsis, systemic inflammatory response syndrome, or bacteremia and are of disease-prognostic value (25–26).

Enocsson et al. studied the plasma suPAR levels of 198 systemic lupus erythematosus (SLE) patients and determined significantly elevated suPAR levels compared to the healthy control group. At the same time, they determined a strong association between systemic suPAR levels and organ damage (27).

Another study on 89 SLE patients carried out by Toldi et al. also determined higher suPAR serum levels compared to the control group and claimed that this can be used as a marker to determine patients with high disease activity (28).

In a study by Kasperske-Zajac et al. examining patients with atopic eczema / dermatitis syndrome (AEDS), the uPA and suPAR levels of moderate and severe AEDS patients did not differ from those of healthy controls (29).

Psoriasis is a chronic, relapsing, inflammatory, and hyper-proliferate skin disease with an unclear etiology. Parameters showing the inflammatory process activation in order to follow the clinical course and to develop treatment strategies are important (30–31). Currently, there are no widely recognized laboratory markers determining disease activity.

To the best of our knowledge, there are no studies investigating suPAR levels in psoriasis patients.

Despite the reports on elevated systemic suPAR levels in various inflammatory diseases, in this study there was not a statistically significant difference in the plasma suPAR levels of psoriasis patients and the healthy control group. Likewise, a statistically significant correlation between plasma suPAR levels and PASI scores in psoriasis patients could not be detected. The underlying reason might be that the study group consisted of mild- to moderate-level psoriasis patients.

Conclusion

SuPAR levels, a potential useful biomarker in demonstrating disease severity and risks of possible comorbidities in future, must be further researched with larger patient series and in psoriasis patients with higher PASI scores.

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