ORIGINAL ARTICLE

Evaluation of serum lipocalin-2 level in patients with plaque psoriasis and its correlation with PASI score

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ABSTRACT

Background: Psoriasis is a chronic papulosquamous disease with variable morphology, distribution, severity, and clinical course, affecting approximately 2% of the population. Lipocalin-2 is expressed in liver, lung, kidney, macrophages and epithelial cells. The lipocalin-2 is known to be related to insulin resistance, obesity and atherosclerotic diseases. Lipocalin-2 expression reflects the different status of inflammation, and may be related with the epidermal hyperplasia.

Objective: The aim of this study was to determine the relationship between serum lipocalin-2 level and severity of psoriasis vulgaris.

Subjects and Methods: A case-control study was carried out on forty patients with plaque psoriasis and forty age and sex matched healthy controls. Full history, general and dermatological examinations was done for all patients and controls. Height, weight, BMI, blood pressure and serum lipocalin-2 were estimated for both patients and controls.

Results: The mean serum level of lipocalin-2 was 112.7±12.8 ng/dl in psoriatic patient and 66.7±8.7 ng/dl in control group with a statistically significant elevation in psoriatic patient than control group (P value<0.001). No significant correlation was found between serum level of lipocalin-2 and PASI score, duration of disease and BMI.

Conclusion: Serum lipocalin-2 level in patients with psoriasis vulgaris was significantly higher than those in healthy controls, and no correlation between serum level of lipocalin-2 and PASI score was identified.

KEY WORDS: lipocalin-2, psoriasis, PASI

INTRODUCTION

Psoriasis is a chronic autoinflammatory immune mediated disease of the skin and joints.[1] It can have a significant negative impact on the physical, emotional, and psychosocial well being of affected patients.[2] It affects approximately 2% to 3% of the total population.[3] Most scientific research refers to the common clinical variant termed psoriasis vulgaris, which affects approximately 85 to 90% of all patients with the disease. Psoriasis patients have a natural history of outbreaks followed by temporary remissions.[4] The pathogenesis of psoriasis can be considered in the context of 3 phases: Phase I is the interaction between genetic and environmental factors, Phase II is an interaction between innate/adaptive immunity and the resident skin cells, Phase III consists of epidermal and dermal remodeling.[5]

Lipocalin-2 has been identified as an adipokine. It is expressed in liver, lung, kidney, macrophages and epithelial cells. The protein lipocalin-2 is known to be related to insulin resistance, obesity and atherosclerotic diseases.[6] Lipocalin-2 expression appears to be regulated by a variety of stimuli through mainly the NF-κB pathway. Lipocalin-2 expression and secretion can be stimulated by TNFα, IL-1β, or IL-6.[7] The

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interaction between adipocytokines like lipocalin-2 and chronic skin and systemic inflammation in psoriasis can be bi-directional. Th1 and Th17 lymphocyte activation in psoriasis is a shared pathway with adipokine activation.[8]

Lipocalin-2 expression reflects the different status of inflammation, and related with the epidermal hyperplasia. As lipocalin-2 is confined to spatially distinct subpopulations of keratinocytes underlying areas of parakeratosis, suggests that the onset of keratinocyte differentiation may be a trigger for high induction of lipocalin-2 expression.[9]

SUBJECTS AND METHODS

Study Population

A case-control study was carried out on forty patients with plaque psoriasis. In addition, the study also included a control group, which consists of another forty, age and sex matched healthy subjects. The patients and control were selected from the Dermatology outpatient clinic, Al Hussein University hospital, faculty of medicine, Alazhar University.

Exclusion criteria: Patients with autoimmune diseases, obesity, hypertension, diabetes mellitus, cardiovascular diseases, cancer and psoriatic patients receiving any topical or systemic treatment for at least one month prior to inclusion in this study.

Patient and control evaluation

Full history, general and dermatological examinations were obtained from all patients and controls. Height, weight, BMI, and blood pressure were estimated for both patients and controls. Diagnosis of psoriasis was made on clinical basis. The extent and the severity of the disease were assessed using Psoriasis Area and Severity Index (PASI) score. Serum lipocalin-2 was measured using ELISA kit supplied by Quantikin, R&D Systems, and Minneapolis, USA.

Statistical analysis

The collected data were coded, entered, analyzed and tabulated. Data were statistically described in terms of mean ± standard deviation (± S.D), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using (unpaired Student t test) for independent samples in comparing 2 groups when normally distributed. For comparing categorical data, chi square (x2) test was performed. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for Social Science; SPSS Inc., Chicago, IL, USA) version 17 for Microsoft Windows.

RESULTS

This study included forty patients with psoriasis vulgaris. Forty age and sex matched healthy controls were also included in this study. Patients' demographic data, duration of disease, percentage of skin affection and PASI score as shown in Table 1. There was no significant difference in the demographic data between two study groups (Cases and Control). The serum level of lipocalin-2 was significantly elevated in psoriatic patient than control group (P value <0.001). In psoriatic patient, no significant correlation was found between serum level of lipocalin-2 and PASI score, duration of disease and BMI (Ta-

bles: 2, 3 and Fig. 1).

The age of the patients in the two groups ranged from 26 to 63 years. In group A (psoriasis) the mean age (in years) was 44.5±11.2. While, in group B (control) the mean age was 40.2±9.6. The weight of patients (in kilograms) in group A had a mean of 67.9±10.6, while in group B the mean weight was 65.3±11.5, The height of patients (in centimeters) in group A had a mean of 165.5±8.15, while in group B the mean height was 164.2±9.7. There were 18 mails and 22 females in group A. While, in group B there were 21 males to 19 females. The BMI in group A had a mean of 24.6±2. While, in group B it was 24.2±2.3.

The serum level of lipocalin-2 in mild psoriasis was 118+13.41. While, in moderate severity lipocalin-2 level was 107+11.53, and in severe cases level was 115+11.8 with no significant statistical difference (P ≈0.05).

No significant correlation was found when correlating serum levels of lipocalin-2 in patients with their PASI score, duration of disease and BMI.

Table 1 Demographic data, disease duration, PASI and percentage of skin affection presented as mean ± SD

	Psoriasis group	Control group	
	(A) (n=40)	(B) (n=40)	P value
Gender (male/ female)	18/22	21/19	0.24
Age (yrs)	44.511.2±	40.2±9.6	0.07
Weight (kg)	67.910.6±	65.3±11.5	0.282
Height (cm)	165.58.15±	164.2±9.7	0.518
BMI	24.62±	24.2±2.3	0.419
Disease	6.5±5.3	0	
Duration (years)			
PASI score	17.5±9.8	0	
Skin affection	32.1±17.2%	0	

Table 2 Serum lipocalin-2 level in psoriasis and control group

	Lipocalin-2-2 (ng/dl)	
	Patients	Control
Range	84-142	54-84
Mean	112.7±	66.7
+SD	12.8	8.7
t. test		
p. value		

*= significant difference between psoriasis and control group regarding serum lipocalin-2

Table 3 Serum lipocalin-2 level in different groups of psoriasis severity

Severity of Psoriasis	Lipocalin-2-2 (pg/Ml)			
	Mean	+SD	N	P. value
Mild	118	13.41	11	
Moderate	107.06	11.53	17	0.05
Severe	115.75	11.8	12	

Table 4 Correlation between serum level of lipocalin-2 and PASI scores, disease duration and BMI in psoriatic patients

	Patients	
	Serum lipocalin-2	
	Correlation coefficient(r)	(p-value)
PASI score	-0.009	0.955
Duration (yrs)	0.098	0.547
BMI	0.082	0.462

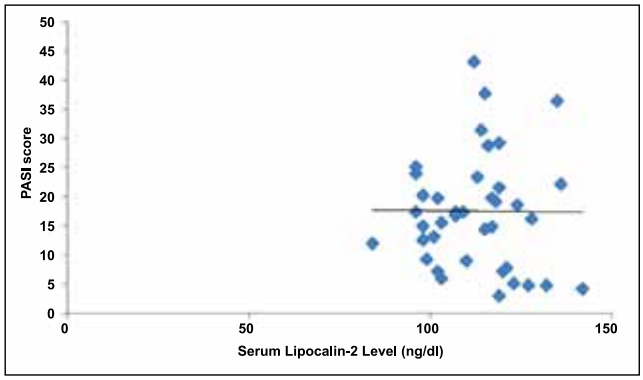

Fig. 1 Correlation between serum lipocalin-2 level in patient group and PASI score with no significant correlation.

DISCUSSION

Psoriasis vulgaris is an inflammatory immune-mediated disease. The lesional skin is characterized by sharply demarcated, erythematous scaly plaques.[10] It can have a significant negative impact on the physical, emotional, and psychosocial well being of affected patients.[2] Psoriasis shows multifactorial etiology and polygenic genetic transmission. It is considered that numerous proinflammatory cytokines, such as TNF-alpha, IL-1, IL-2, IL-6, IL-8, and IL-12, have the main role on the pathogenesis and they are secreted by T cells infiltrated in the skin, in response to unspecified antigenic stimulus. On the other hand, keratinocyte proliferation is a secondary biological phenomenon.[11]

Lipocalin 2, also known as neutrophil gelatinase-associated lipocalin, is a 25 kDa protein. Lipocalin-2 has been defined as an adipokine. It is expressed in liver, lungs, and kidneys, as well as adipocytes, macrophages, and epithelial cells.[6] Lipocalin-2 is an antimicrobial protein.[12] It is stored in specific granules of the human neutrophil and functions as a modulator of inflammation.[11] Lipocalin-2 has been demonstrated to be a proinflammatory molecule causing some to call it a cytokine. Lipocalin-2 expression is upregulated in various acute and chronic inflammatory diseases such as psoriasis, eczema, periodontitis, and myocarditis.[13] Lipocalin-2 might be a link between psoriasis and its comorbidities.[14]

The present work declared a significant higher serum lipocalin-2 compared to healthy control. Also Baran et al., 2016,[14] Kamata et al., 2012,[6] Ataseven et al., 2014,[11] Gul et al., 2014[15] and Coimbra & Santos-Silva 2014[16] have found similar results. However, a study by El-Hadidi et al., 2013[17] did not show significant differences in lipocalin-2 levels compared to controls, it can be attributed to heterogeneity in the study designs, non-standardized laboratory techniques and the inclusion of psoriatic patients with variable severity and inflammatory profiles and inclusion of metabolic syndrome and obesity but in our study, metabolic syndrome and obesity were excluded and our sample size was larger, also difference in sex, age or race must be taken in consideration.

In the present study there was no correlation between serum lipocalin-2 and PASI scores. There are conflicting results regarding the correlation between lipocalin-2 and PASI. In agreement with our results, Baran et al., 2016[14] also found no correlation between serum lipocalin-2 and PASI. Unlike our findings, Romani et al., 2012,[18] reported a positive correlation between baseline serum lipocalin-2 and PASI score. These differences can be attributed to several factors. One of the main causes is the fact that lipocalin-2 is secreted from various tissues, such as liver, lungs, and kidneys, as well as adipocytes, macrophages, and epithelial cells. Other factors, such as the diversity of patient groups consisting of individuals with different disease durations and severities, past medical history, and medical therapies, may also explain the conflicting results.

In our study there was no correlation between serum lipocalin-2 and the duration of psoriasis, unlike our results, Baran et al., 2016[14] reported a significant positive correlations between lipocalin-2 and disease duration. These differences can be attributed to inclusion of psoriatic patients with variable severity in our study and exclusion of metabolic syndrome and obesity.

Conclusion and Recommendations

Serum lipocalin-2 levels in patients with psoriasis were significantly higher than those in

healthy controls. There was no correlation between serum lipocalin-2, PASI score and duration of the psoriasis. Validation with a larger study population, comparing serum lipocalin-2 in patients with psoriasis and the general population is needed.

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