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Chemerin: An Adipokine Involved in Pathogenesis and Severity of Psoriasis Vulgaris

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# **ABSTRACT:**

**Background:** Chemerin, a member of the adipokine family, plays a unique role in the inflammatory process of many chronic inflammatory diseases through modulating the synthesis of many inflammatory cytokines and the activity of some immune cells. This study aimed to clarify the possible role of serum chemerin in the pathogenesis and disease severity in patients suffering from psoriasis.

**Methods:** 45 psoriasis patients and 45 matched healthy controls were included. Using ELISA, serum chemerin levels were assessed in all participants along with a complete lipid profile. Psoriasis severity was investigated using the Psoriasis Area and Severity Index (PASI).

**Results**: Patients had a considerably higher serum chemerin level than controls (P <0.001). The PASI scores showed a positive correlation with chemerin levels (r =0.660, P =0.007). Compared to their matched controls, psoriasis patients had a statistically higher mean BMI (P <0.001). Higher TGs, TCs, and LDL in patients compared to controls were also indicative of a disordered lipid profile (P <0.001).

**Conclusions:** The fact that psoriasis patients have higher levels of chemerin than healthy controls raises the possibility that it might be influencing the course of the disease. Lipid profile results suggest that dyslipidemia may have contributed to its development, and chemerin may be a viable adipokine marker of the onset of metabolic syndrome in such patients.

Keywords: Chemerin; Psoriasis; Metabolic; BMI

#### **INTRODUCTION**

A member of the adipokine family, chemerin has been linked to inflammation and is important in regulating a variety of physiological and pathological processes. Chemerin promotes the production of pro-inflammatory substances such TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and IL-8. Additionally, it has a role in the final stage of the inflammatory response. It promotes NK-cell recruitment and improves apoptotic cell phagocytosis [1, 2].

Additionally, it affects the pathogenesis of metabolic syndrome, which includes coronary atherosclerosis, ischemic stroke, obesity, and type II diabetes. It contributes in a special way to the

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inflammatory process of numerous chronic inflammatory skin diseases [3].

Psoriasis is a chronic inflammatory skin condition that is mediated by the immune system and significantly impairs the quality of life. It is seen as a systemic disease that lowers life expectancy and has neurological, metabolic, cardiovascular, and articular effects [4]. Psoriatic skin fibroblasts were shown to express more chemerin than fibroblasts from healthy individuals or those with uninvolved skin. When the disease was active, its expression was higher; when it was in remission, it was lower [5]. In this case-control study, we clarified the possible role of serum chemerin in the pathogenesis and disease severity in patients suffering from psoriasis.

## METHODS

Ninty participants of both sexes were included. They were divided into two equal groups: Group A, which included the psoriasis patients and group B, which included the age and sex-matched, seemingly healthy controls. Participants in the study were excluded if they had diabetes mellitus, a collagen vascular disease, a neoplastic condition, an autoimmune disease, a hepatic condition, or a renal condition.

According to our criteria, women who were pregnant or breastfeeding were also disqualified. The control group shouldn't have a history of inflammatory skin conditions. Our work was approved by Zagazig University's institutional review board (IRB) in Egypt. At the beginning of the study, the patients gave their informed consent.

Every patient underwent a full history taking, general examination, and extensive dermatological examination. Three groups were created based on the body mass index (BMI): normal (18.5-24.9 kg/m2), overweight (25-29.9 kg/m2), and obese (>30 kg/m2).

Following a 12-hour fast, five milliliters of venous blood were extracted from each participant and placed into plain tubes. After allowing the tubes to clot, the serum was separated using an HITACHI himac CT6E® centrifuge set at 3000 rpm for 15 minutes. Serum samples were stored at -20 °C before assaying. According to the guidelines provided by the manufacturer (http://www.sunredbio.com), serum chemerin was estimated using the human Chemerin ELISA Kit (Sunred Biotechnology Company, catalogue no.: 201-12-01436; China).

Using an automated analyzer (Cobas 8000 platform-720 module), triglycerides (TGs), total cholesterol (TC), high-density lipoprotein (HDL), and lowdensity lipoprotein (LDL) were measured as components of the full serum lipid profile.

According to the psoriatic area severity index (PASI), a score of less than 7 indicates mild psoriasis, while a score of more than 15 indicates severe psoriasis.

## STATISTICAL ANALYSIS

To analyze the data, SPSS (IBM Corporation, Armonk, NY) version 20 was utilized. ANOVA (F-test), independent t-test, independent Chi-square test (X2), and Pearson correlation coefficient. The 5% level was chosen as the significance threshold. P-values below 0.05 were considered statistically significant. The more significant the outcome, the lower the P value.

### RESULTS

There were 21 females and 24 males with psoriasis among the 90 study participants. Age and sex differences between the cases and controls were not statistically significant (Table 1). Compared to their matched controls, psoriasis patients had a considerably higher mean BMI (P <0.001) (Table 1). Additionally, patients had statistically greater serum chemerin levels than controls (P <0.001) (Table 1). As for the lipid profile measures, there was no significant difference between the two groups in terms of the HDL value (P = 0.278), but TGs, TCs, and LDL were statistically greater in cases than controls (P = 0.005, 0.04, and 0.007, respectively).

In the psoriasis group, serum chemerin only varied significantly between mild cases on one hand, and moderate and severe cases on the other hand (p < 0.01) (Table 2) (Figure 1). Likewise, BMI didn't significantly differ according to the degree of severity of the disease (p=0.963). lipid profile markers: TGs, TC, LDL, and HDL didn't differ significantly according to the degree of severity (P= 0.125, 0.889, 0.611, and 0.283 respectively) (Table 2).

Serum chemerin was found to be statistically significantly correlated with the disease's duration, severity, and PASI score (Figure 2, Supplementary table). According to Receiver Operating Characteristic curve (ROC) study, the area under the ROC curve for chemerin's overall diagnostic performance in AV patients was 0.981 (P=0.000, 95% CI 0.948-01.00). With a sensitivity of 96.7% and a specificity of 100%, the cutoff value for predicting acne vulgaris was 1993.6ng/ml (Table 3, Figure 3).

Variable		psoriasis group N= 45	<b>Control Group</b> N=45	Р
Age		41.47±13.74 (20-67)	21.0±4.07 (18-30)	<0.001
Gender Male		24 (53.3%) 21 (46.7%)	15 (33.3%)	0.271
Female           BMI (Kg/m²)		28.1±5.9 (18.9-42.9	30 (33.7%) 22.49±0.86 (20.7-23.6)	<0.001
Duration of the disease		3.35±4.07 (0.58-15)	-	
PASI		11.21±15.69 (1.8-49.9)	-	
Serum Chemerin (ng/ml)		2833.25±651.2	1588.1±827.44	<0.001
Lipids         TGs (mg/dl)           TC (mg/dl)		126.63±57.31	73.65±23.23	<0.001
		189.77±36.35	132.7±15.49	<0.001
	LDL(mg/dl)	113.67±34.2	69.44±13.03	<0.001
	HDL(mg/dl)	49.86±9.56	48.58±4.24	0.27

Table 1: Demographic, clinical and laboratory data of participants

One-Way ANOVA & \* Chi square test are used to analyze the difference between the groups. P<0.005 is significantly different. N: number. GACS (Global Acne Grading System). TGs: triglycerides, TC: total cholesterol, LDL: low density lipoprotein, HDL: high density lipoprotein.

		Degr				
Variables		Mild	Moderate	Severe	Р	
		n=23	n=14	n=8		
Age (years)		38.13±14.14	45.42±13.35	44.12±9.81	0.232	
BMI (Kg/cm <sup>2</sup> )		27.84±5.89	28.36±6.98	28.30±4.29	0.963*	
Duration of the disease (years)		2.17±2.18 <sup>a</sup>	1.69±1.03 <sup>ab</sup>	12.0±4.24°	0.003	
Family Positive		8 (34.8%)	4 (28.6%)	0 (0%)	0.156*	
history	Negative	15 (65.2%)	10 (71.4%)	8 (100%)	0.130	
Itching	Positive	23 (100%)	14 100%)	8 (100%)		
Ittillig	Negative	0 (0%)	0 (0%)	0 (0%)		
PASI Score		7.35±7.41	21.49±15.86	54.8±9.41	<0.001	
Serum chemerin (ng/ml)		2408.25±368.13	3244.4±715.16	3335.63±264.1	<0.010*	
TGs (mg/dl)		116.62±48.44	152.3±71.59	110.52±42.55	0.125	
TC (mg/dl)		191.66±42.59	185.78±33.11	191.30±22.87	0.889*	
LDL (mg/dl)		117.06±40.73	106.02±30.59	117.35±15.23	0.611	
HDL (mg/dl)		47.91±9.08	50.69±10.89	54.02±7.87	0.283	

'One-Way ANOVA & \* Chi square test are used to analyze the difference between the groups. P<0.05 is significantly different. N: number, TGs: triglycerides, TC: total cholesterol, LDL: low density lipoprotein, HDL: high density lipoprotein. GAGs (global acne score system). BMI (body mass index).

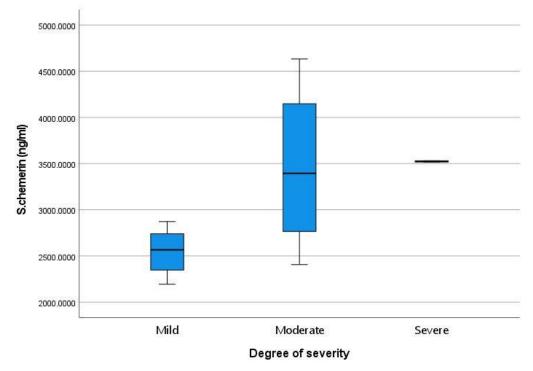


Figure 1: Serum chemerin concentration in various psoriasis severities.

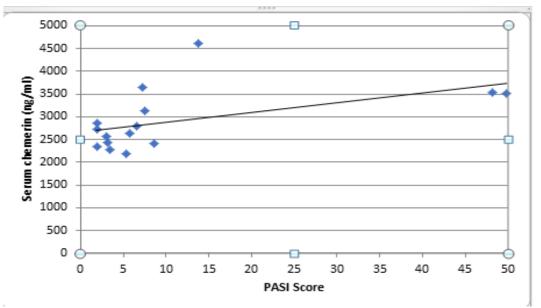
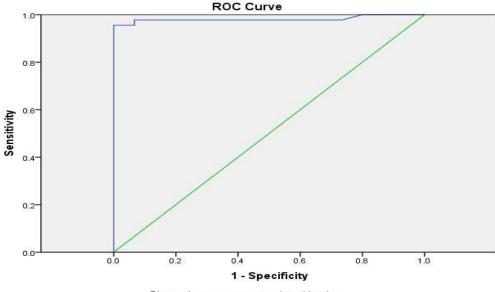


Figure 2: correlation between serum chemerin concentration and PASI in psoriasis patients.

Table 3: ROC analysis for detecting the ability of serum chemerin to predict Psoriasis

Cut-off value	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval		
ng/ml	mcu		noymptotic org.	Lower Bound	Upper Bound	
≥1993.6	0.981	0.017	0.000	0.948	1.000	



Diagonal segments are produced by ties.

Figure 3: Roc curve of serum chemerin to distinguish psoriasis patients from normal subjects

### DISCUSSION

Understanding the pathophysiology of chronic inflammatory skin disorders is still researchable. Blood levels of certain adipokines were found to be correlated with the severity of some dermatoses [6]. Chemerin, a member of which, has a role in different stages of inflammation and a unique role in many chronic inflammatory dermatoses [7, 8]. Serum concentration of chemerin was found to be positively correlated to the concentration of many pro-inflammatory cytokines e.g. IL-6, TNF-α and CRP. Moreover, chemerin has an influence on the pathophysiology of metabolic syndrome [9, 10, 11]. Obesity has been found to be a major problem related to many chronic inflammatory dermatoses as acne vulgaris, atopic dermatitis, and psoriasis. Obesity creates pro-inflammatory mediators that have a local and a systemic impact on those diseases.

Similar to many other studies [12-15], we observed that serum chemerin was significantly higher in psoriasis patients than the control group. So, we suppose that chemerin may be a unique diagnostic marker for psoriasis and a tool to assess the efficacy of various anti- psoriasis therapies.

Contrary to our study, it was found that patients with psoriasis and psoriatic arthritis had significantly reduced levels of circulating chemerin than healthy controls [16]. This difference may be explained as they excluded any patients with obesity or metabolic syndrome from their study, while in our study we aimed to find the association of the disease with those conditions.

Unlike our results, Tekely et al. [14] found no significant correlation between serum chemerin and PASI score as in our study. However, other studies [12, 13] showed a positive correlation between them. This difference may be due to different sample sizes. Meanwhile, Borsky et al. [15], found a significant negative correlation between chemerin and PASI. This difference needs to be researched. Chemerin had significantly higher expressions in the psoriatic tissues than in non-psoriatic ones and it was shown to be strongly connected with PASI score as well [17].

Our results clarified, with no doubt, that serum chemerin level rises significantly in severe psoriasis, and this high level is most probably closely related to its etio-pathogenesis and the initiation of the consequent mutual inflammatory cascade via release of cytokines IL-6 and IL-22 from TH17.

## CONCLUSIONS

The high level of serum chemerin level was associated with some other high levels of key parameters of the metabolic syndrome suggesting that chemerin might be an independent promising adipokine marker of metabolic syndrome. Further research is necessary to confirm these findings on a larger scale of patients from different ethnicities. Moreover, measurement of serum chemerin level could be used as a diagnostic marker for psoriasis. Assessing serum chemerin levels before and after different treatment regimens may help in choosing the most appropriate approach of **Funding sources:** None

Conflicts of interest: None declared.

IRB approval status: reviewed and approved by Zagazig University Hospitals

**IRB approval** #9327 date: 22-2-2022.

All patients gave consent with the understanding that this information may be publicly available.

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# Supplementary data:

 Table 1 (Supplementary): Correlation of serum chemerin concentration with some selected variables in psoriasis patients and controls:

Variable	Psoriasis group		Control group	
	r	р	r	р
Age	0.178	0.243	-0.144	0.346
BMI	0.001	0.995	0.349	0.01
Duration	0.339	0.02	-	-
Severity	0.660	0.007	-	-
PASI score	0.318	0.03	-	-
TGs	0.292	0.052	0.073	0.639
ТС	0.235	0.120	-0.433	0.003
LDL	0.121	0.427	-0.379	0.01
HDL	0.244	0.106	0.261	0.083

Correlation is analyzed using Pearson's correlation coefficients. P is significant if <0.05. TGs: triglycerides, TC: total cholesterol, LDL: low density lipoprotein, HDL: high density lipoprotein. BMI (body mass index).

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