Tissue Expression of Visfatin in Psoriatic Patients

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Abstract:

Background: Psoriasis is a chronic disease, in which genetic, immunological, and environmental factors play a significant role. The immunological mechanism involved in pathogenesis causes cutaneous inflammation and keratinocytes hyperproliferation. Subcutaeous adipose tissue secretes adipokines which play a role in cutaneous inflammation. Visfatin is an adipokine that induces inflammatory process by increasing cytokines production and activation. It affects inflammatory and immune response through induction of chemotaxis. **Aim of this work:** To estimate visfatin level in lesional tissues of psoriatic patients in comparison with healthy controls and its correlation with disease severity. **Patients and Methods:** The expression of visfatin was detected in the skin of 30 psoriasis patients and 30 healthy controls using using ELISA technique. **Results:** Visfatin expression was significantly higher in psoriasis patients compared to healthy controls. In addition, there was no significant difference between visfatin expression and severity of the disease. **Conclusion:** Visfatin may play a role in pathogenesis of psoriasis.

Keywords: Psoriasis, Visfatin, expression.

1. Introduction:

Psoriasis is a common, chronic, recurrent, immune mediated skin disease that affects approximately 2% of the population. It is a papulosquamous disease characterized by well demarcated, symmetrical, circular, erythematous papules plaques with silvery-white dry scales. Common affected sites include the scalp, elbow, knee, lumbosacral area and skin folds (1).

The most common clinical variant of psoriasis; psoriasis vulgaris represents around 85-90% of

all patients with the disease. Other clinical types include guttate, pustular and erythrodermic psoriasis. Several comorbidities of psoriasis are identified including depressive illness, cardiovascular disorders and psoriatic arthritis (2).

Psoriatic patients have associated nail affection in about 50% of cases that commonly manifested by pitting, onycholysis and hyperkeratosis. This involvement is an important marker of disease severity (3).

Histopathological picture of psoriasis exhibits epidermal psoriasiform hyperplasia, acanthosis, keratinocytes proliferation with parakeratosis and vascular hyperplasia.There is infiltration of T-lymphocytes, neutrophils and other inflammatory cells in lesional areas (4).

Although the exact etiology of psoriasis is not yet fully known, multiple immunological factors contribute to its pathogenesis. The immunological mechanism involved in pathogenesis causes cutaneous inflammation and keratinocytes hyperproliferation. Subcutaeous adipose tissue secretes adipokines which play a role in cutaneous inflammation (5). One of these adipokines is Pre B cell Colony Enhancing Factor (PBEF); visfatin. Visfatin is an adipocytokine synthesized by adipose tissue and its plasma levels are parallel to amount of visceral fat, however its gene expression is more apparent in visceral fat than sc fat (6).

It plays a role in immune and inflammatory function. Many inflammatory disorders are associated with increased plasma levels of visfatin and its mRNA expression as in crohns disease and ulcerative colitis (7).

Serum visfatin levels may be upregulated in response to pro-inflammatory cytokines secreted during inflammation. Furthermore, visfatin itself induces inflammatory process by increasing cytokines production and activation (8). The potential role of visfatin in psoriasis could be explained by affection of inflammatory and immune response through induction of chemotaxis and increase production of cytokines such as IL-1, IL-6 and TNFα (9).

2.Patients and Methods:

Study population:
The present study included 30 Egyptian patients with chronic plaque psoriasis who had not received psoriasis treatment for at least three months before biopsy. Patients were included from both sexes, their age ranged from (20-50 years). They were recruited from dermatology outpatient clinic at Beni-Suef University hospital. Thirty healthy controls were chosen randomly from any other outpatient clinics that were proven to be healthy with no family history of psoriasis.

Informed consent was obtained from the participants in this study after ethical committee approval from Dermatology Department, Faculty of Medicine at Beni-Suef University. Patients were chosen randomly according to inclusion and exclusion criteria.

Inclusion criteria:

- Age between 20 to 50 years old.
- A diagnosis of mild to severe psoriasis for at least 6 months prior to baseline.
- Patients not receiving psoriasis treatment for at least three months.
- Both males and females were included.

Exclusion criteria:

- Patients diagnosed with acute infection at time of sample taking.
- Patients with proven other autoimmune diseases.
- Patients with systemic or other dermatological diseases.
  Controls were chosen randomly from other outpatient clinics.

Data collection methods:

1) **Detailed history**
a. Age and sex of patients.
b. Onset of the disease.
c. Course of illness.
d. Duration of disease.
e. Family history.
f. History of precipitating factors.

2) **Clinical examination:**
a. To determine the type of psoriasis.

b. Assesment of disease severity using PASI score.

3) **Estimation of the levels of visfatin:**

Tissue samples were collected by punch biobsy, (4mm in diameter), from lesions, (psoriatic areas) and normal skin from the healthy controls. These samples were preserved in sterilized tubes in frozen state at -20^0C until assayed using ELISA technique.

Statistical analysis:

- The collected data were coded then entered and analyzed using the SPSS version 22 (Statistical package for social science).

- Descriptive statistics for the socio-demographic characteristics of Participants, and detailed patient history were first analyzed:

- Description of qualitative variables by frequency and percentage.

- Description of quantitative variables in the form of mean and standard deviation (mean ± SD).

- Graphs were used to illustrate simple information.

- Suitable statistical tests were used (Chi-square (χ^2), one way ANOVA, one sample t-test, Person's and Spearman's correlation), P-values equal to or less than 0.05 were considered statistically significant.

- According to assessment of psoriasis severity among the studied group, more than half of patients presented by mild disease (60%), and 16.7% of patients presented by moderate disease while 23.3% presented with severe disease.

Grades	Number (n)=30	Percent (%)
Mild (PASI<7)	18	60.0
Moderate (PASI 7-12)	5	16.7
Severe (PASI >12)	7	23.3

Table (1): Grades of disease severity among the studied psoriasis group.

The Laboratory characteristics of the patient:

The expression of visfatin in cases ranged from 3.8 to 17.9, with mean value of (11.5 ± 3.3). While in controls, it ranged from 1.9 to 9.1, with mean value of (4.73 ± 2.36). The expression of visfatin was significantly higher in psoriasis group rather than in the control one, with p value (<0.001).

Visfatin	Psoriasis group	Control group	P value
Mean ± SD	11.5± 3.3	4.73 ± 2.36	< 0.001*
Minimum	3.8	1.9	
Maximum	17.9	9.1	

Table (2): Serum level of visfatin among the studied groups.

P value ≤ 0.05 is considered significant

The cut off value of visfatin (to be used as a predictor of psoriasis) was > 9.035 with high sensitivity and specificity (80%, 87% respectively) (**Figure1**).
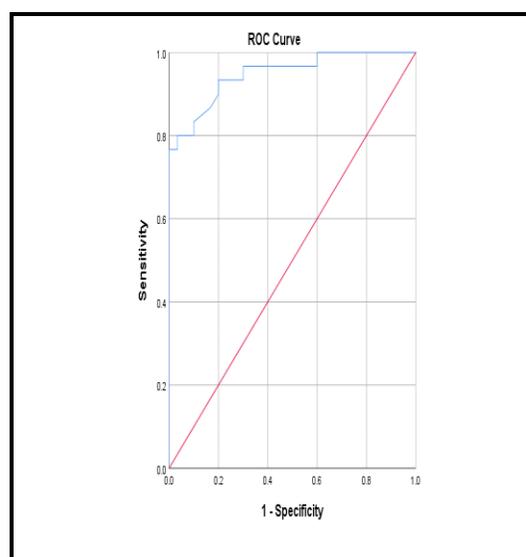

Figure 1 - ROC curve between (Psoriasis and Control) groups regarding Visfatin expression.

	GDF-15-
AUC	0.948
P value	<0.001[*]
95% C.I	0.896-1.000
Cut off	<9.035
Sensitivity	80%
Specificity	87%

Table (3): Sensitivity and specificity for visfatin to predict psoriasis cases versus control.

Regarding severity of the disease, there was no statistically significant difference between patients with different disease grades according to PASI score in the expression of visfatin (p value = 0.898).

PASI (Psoriasis Area and Severity Index)	Visfatin level (Mean± SD)	P value
Mild (n=18)	11.65± 3.02	
Moderate (n=5)	11.68± 4.54	0.898
Severe (n=7)	10.97± 3.59	
Total (n=30)	11.50± 3.31	

Table (4): The distribution of the psoriatic patients as regards to disease severity and visfatin level

There was no statistically significant difference between the different age groups and different sex regarding visfatin level, p value 0.667 and 0.711 respectively.

Demographic characteristics	Visfatin level (Mean± SD)	P value
Age groups	10.91± 2.05	
>30	11.36± 4.17	0.667
30-50	11.96± 2.11	

	Visfatin level (Mean± SD)	P value
<50		
Sex		
Male	11.67± 3.15	
		0.711
Female	11.20± 3.70	

Table (5): The distribution of the studied psoriasis group as regards demographic characteristics and visfatin level .

Regarding family history, there was no statistically significant difference between patients with positive family history for the psoriasis disease and patients with negative family history for the disease (p value = 0.974).

Family history	Visfatin level (Mean± SD)	P value
Positive (n=4)	11.45± 2.91	
Negative (n=2	11.51± 3.42	0.974
Total (n=30)	11.50± 3.31	

Table (6): The distribution of the studied psoriasis group as regards to Family history of the disease and visfatin level.

Regarding onset of the disease, there was no statistically significant difference between patients with sudden onset and patients with

gradual onset of the disease in visfatin level (p value = 1.000).

As regards course of the disease, there was also no statistically significant difference between patients with different courses of the disease in visfatin level (p value = 0.405).

While there was statistically significant difference between patients with different durations of the disease in visfatin level (p value = 0.025).

Past history	Visfatin level (Mean± SD)	P value
Onset	11.50± 1.84	
Sudden (n=2) Gradual (n=28)	11.50± 3.41	1.000
Course Progressive (n=7) Regressive (n=2) Stationary (n=4) Remission & exacerbation (n=17)	12.63± 2.61 13.65±0.07 9.66± 5.94 11.22± 2.93	0.405
Duration (months) (n=30)	11.50± 3.31	0.025*

Table (7): The distribution of the studied psoriasis group as regards to past history of the psoriasis disease and visfatin level.

*P value > 0.05 is considered significant

3. Discussion:

Psoriasis is a multisystem immune-dependent inflammatory disease which is developed from immune-mediated mechanisms characterized by disruptions in key cytokines and is accompanied by many comorbidities (10).

Psoriasis is characterized clinically by red, heavily scaled skin plaques containing dense infiltrates of T cells, macrophages, and DCs. The activated T cells release TNF-α, IFN-γ, IL-6, Il-1b and other cytokines, which induce a wide variety of responses as leukocyte migration to inflammatory regions and vasodilation that results in the erythema that is characteristic of psoriatic lesions (11).

Adipose tissue is known to be an active endocrine organ regulating body metabolism by secretion of metabolically important proteins called adipokines. Visfatin is is one of these adipokines that plays a role in the development of early stage B cells. It exhibits an anti-apoptotic effect (12).

Visfatin synthesis is regulated by several factors, including glucocorticoids, TNF and IL-6. It has several pro-inflammatory and immune-modulating properties as visfatin promotes T-cell activation (13).

Studies that evaluated visfatin level in plasma and different tissues revealed that plasma visfatin level correlated significantly with

visfatin mRNA expression in visceral fat. However, no significant correlation was found between circulating visfatin and visfatin mRNA expression in subcutaneous tissue (14).

Psoriatic skin is harboring a lot of inflammatory cells including neutrophils, granulocytes and monocytes which are major sources of visfatin. They might be denounced for such an increase in patients (15).

Since, psoriatic skin controls the ingoing inflammatory process. Thus; it is more likely expressing the highest adipokine levels in opposition to serum (16).

Many previous studies had assessed serum level of visfatin in psoriatic patients, but few researches were conducted to estimate visfatin in lesional psoriatic tissues. Therefore, this study aimed to detect the expression of visfatin in psoriatic skin of diseased patients as compared to normal control persons to investigate the possible role of visfatin in the pathogenesis of this disease. In this study; the average psoriatic patients' age was 46.13 ± 13.87 (SD) years with no statistically significant difference between cases and control groups regarding age and sex as p value (0.580 and 0.301) respectively, That was reported previously as the disease can occur in all age groups but it usually arises in adulthood, in males and females equally (17).

In another report, no statistically significant differences were found between patients and controls ($P > 0.05$) regarding age and sex (18). As regards demographic characteristics and visfatin level, there was no statistically significant difference between the different age groups and different sex, (p value 0.667 and 0.711 respectively). Recent study found that four cases only had positive family history (13.3%) and 26 cases (86.7%) had negative family history for the disease which was unsimilar to other studies in this regard as majority of psoriatic patients had positive family history of the disease (19).

This study demonstrated that the expression of visfatin in cases ranged from 3.8 to 17.9 ng/ml, with mean value of (11.5 ± 3.3 ng/ml). While in controls, it ranged from 1.9 to 9.1 ng/ml, with mean value of (4.73 ± 2.36 ng/ml). The expression of visfatin was significantly higher in cases group rather than in the control one, with p value (<0.001). These results were compared with studies that assessed serum and tissue level of visfatin in psoriatic patients to evaluate its role the pathogenesis of the disease. 20 reported that serum and tissue visfatin levels were elevated in psoriatic patients with mean value of (3.42 ± 0.56) and (4.1 ± 1.4) respectively. Whereas in controls, the mean value of its serum and tissue levels were (2.49 ± 0.55) and (3.5 ± 0.67) respectively . They concluded that serum and and tissue levels of

visfatin in psoriasis group were significantly higher than controls (p-value=0.001, 0.04 respectively) (20). 21 found that the serum level of visfatin ranged between 15 and 60 ng/ml, mean 26.6 ± 10.21 ng/ml, in the patient group, whereas in the control group, the serum level of visfatin ranged between 10 and 29 ng/ml, mean 15.6 ± 3.38 ng/ml. The serum level of visfatin was statistically significantly higher in the patient group than in the control group (21).

This was in accordance to 22 who found appositive correlation between psoriatic patients and normal control as regard serum levels of visfatin to noted the role and clinical significance of serum levels of visfatin in patients with psoriasis vulgaris. There was also a significant difference between the active stage and the rest stage of the disease (22).

The disease was evaluated by the Psoriasis Areas and Severity Index (PASI); more than half of patients presented by mild disease (60%), and 16.7% of patients presented by moderate disease while 23.3% presented with severe disease. There was no statistically significant difference between patients with different disease grades according to PASI score in the expression of visfatin (p value = 0.898). Similar findings were found by 23 as no statistically significant correlation was observed between PASI and visfatin levels (P>0.05). But, a statistically significant linear correlation was observed between PASI scores and the TNF-α levels (P=0.009) and no statistically significant correlation was found between the levels of TNF-αand visfatin (p=0.376) (23).

However, 24 found no statistically significant difference in the serum visfatin levels between patients with psoriasis and the control group, but found a slightly positive correlation between visfatin and PASI in patients (24).).

In the current study, there was no statistically significant difference between patients with sudden onset and patients with gradual onset of the disease in visfatin level (p value = 1.000). As regards course of the disease, there was also no statistically significant difference between patients with different courses of the disease in visfatin level (p value = 0.405). While there was statistically significant difference between patients with different durations of the disease in visfatin level (p value = 0.025). Although, another research indicated possible role of visfatin in psoriasis, as a significant higher serum concentration of visfatin was detected in the psoriatic patients (p<0.001) than in the control group. There was a significant positive correlation between serum visfatin concentration and PASI (p = 0.008) and BSA (p = 0.007) (25).

In agreement with this study, 26 measured serum levels of visfatin in patients with psoriasis vulgaris to detect its role in the pathogenesis of the disease. They found that the serum levels of visfatin was significantly higher

than normal controls, and there was a significant correlation between visfatin level and PASI score proposing possible role in disease activity and prognosis (26).

4. Conclusion and Recommendations:

The results of our study suggest that visfatin might play a significant role in the pathogenesis of psoriasis. Lesional visfatin level showed a significant value with duration of the disease in psoriatic patients indicating visfatin as a marker of disease chronicity. No significant correlation was found between visfatin tissue level and severity of the disease. This study may provide important clues to assist in the development of new therapeutic strategies for patients with psoriasis.Further studies are suggested to better understand whether visfatin potentially affects pathogenesis of psoriasis and relation between tissue visfatin level and severity of the disease.

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