



# Study of visfatin expression in acne patients in tissue and serum

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Received: October, 2018  
Accepted: September, 2019  
Published: \*\*\*

## Abstract

**Background:** Acne is a chronic inflammatory disease of the pilosebaceous units, of multifactorial pathogenesis, one of which could be an adipokine such as visfatin.

**Aim:** The aim of this study was to study visfatin expression both in lesional skin and serum, of acne patients versus healthy controls. The secondary aim was to study the relationship of visfatin levels with dyslipidemia/metabolic syndrome.

**Methods:** This study included 30 patients with moderate and severe acne vulgaris and 30 age- and sex-matched healthy controls. Serum and tissue visfatin were estimated by enzyme-linked immune-sorbent assay. Clinical and laboratory examinations were done to assess the anthropometric data and various criteria of metabolic syndrome.

**Results:** Tissue and serum visfatin levels were significantly higher in patients as compared to healthy controls. Tissue visfatin levels were significantly higher than its serum levels in both patients and controls. Serum visfatin was significantly higher in overweight individuals. No correlations were found between tissue and serum visfatin levels in both patients and controls. Moreover, serum and tissue visfatin levels did not correlate to any of the lipid profile parameters or criteria of metabolic syndrome in acne patients.

**Limitations:** The study had a small sample size and did not localize the exact source of tissue visfatin. Polycystic ovary syndrome PCOS was not evaluated.

**Conclusion:** Visfatin is an important proinflammatory adipokine, with significantly higher expression in acne patients. Tissue rather than serum visfatin might play a key role in acne.

**Key words:** Acne, adipokine, visfatin

**DOI:**  
10.4103/ijdv.IJDVL\_856\_18

**PMID:**  
32242871

## Introduction

Acne is a common skin disorder of adolescence with a negative psychological impact.<sup>1,2</sup> The pathogenesis of acne is multifactorial.<sup>3-6</sup>

Visfatin is a 52 kDa protein secreted mainly by visceral fat.<sup>7-9</sup> Its inflammatory role, in coronary atherosclerosis<sup>10</sup> and psoriasis,<sup>8</sup> has been postulated. Recently, visfatin expression was detected at the level of sebaceous gland.<sup>11</sup>

### Aim of work

The aim of this study was to estimate the expression of visfatin in acne patients in both lesional skin and serum

and to compare them with controls. The secondary aim was to correlate the visfatin levels to acne severity as well as dyslipidemia and metabolic syndrome.

## Methods

This study was conducted at the Dermatology Outpatient Clinic, Faculty of Medicine, Cairo University.

In all, 30 acne patients and 30 age- and sex-matched controls of both sexes were recruited in the period between January and June 2017. Inclusion criteria included ages ranging from 11 to 40 years with moderate to severe grades of acne. Patients who received any systemic and/or topical acne

**How to cite this article:** Samir N, Alyafrazi RM, Ashour SS, Shalaby S. Study of visfatin expression in acne patients in tissue and serum. Indian J Dermatol Venereol Leprol 0;0:0.

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treatment in the past 3 months were excluded. In addition, smokers, patients on lipid-lowering agents, and pregnant and lactating females were excluded.

Participants signed informed consents before enrollment, and the study was approved by the research ethical committee of the Faculty of Medicine, Cairo University.

### History and examination

All patients were subjected to thorough history taking and general examination including measuring body weight, height, waist circumference, blood pressure, and body mass index.<sup>12</sup> Acne was graded according to the Global Evaluation Acne (GEA) scale developed by Dréno *et al.* 2011.<sup>13</sup>

Estimation of fasting plasma glucose level and lipid profile (total cholesterol, triglycerides, low-density lipoproteins, and high-density lipoproteins) was done.

### Estimation of visfatin level

Tissue visfatin – Two-mm punch skin biopsies were taken from active acne lesions on the face of patients and normal facial skin in controls.

Serum visfatin – Five ml of peripheral venous blood was collected from each patient and control in plain test tubes, was left to clot, and then was centrifuged at 2500 rpm for 10 min.

Visfatin/NAMPT kit was based on the sandwich enzyme-linked immune-sorbent assay technology.

### Statistical methods

Data were coded and entered using the statistical package SPSS version 24. Comparisons between groups were done using

unpaired *t*-test in normally distributed quantitative variables and nonparametric Mann–Whitney test for non-normally distributed quantitative variables.<sup>14</sup> For comparing categorical data, Chi-square test was performed. Exact test was used when the expected frequency is less than 5.<sup>15</sup> Correlations were done using Spearman's correlation coefficient.<sup>16</sup> *P* values less than or equal 0.05 were considered statistically significant.

### Results

This study included 30 patients with acne vulgaris and 30 sex- and age-matched healthy controls. Patients were 20 females (66.7%) and 10 males (33.3%). Ages ranged from 16 to 33 years with a mean of  $19.53 \pm 4.21$  years. The controls included 22 females (73.3%) and 8 males (26.7%). Ages ranged from 16 to 25 years with a mean of  $19.83 \pm 2.25$  (years). The duration of acne ranged from 3 to 60 months with a mean of  $22.53 \pm 17.15$  months.

### Clinical and laboratory data

Comparison between patients and controls showed the waist circumference to be the only significant variable ( $P = 0.014$ ). Data is summarized in Table 1.

### Visfatin levels

Upon comparing patients and controls, both tissue and serum visfatin were significantly higher in the patient group ( $P \leq 0.001$  and  $0.011$ , respectively) [Table 1]. Tissue visfatin was significantly higher than serum visfatin in both patients and controls ( $P < 0.001$ ) [Figure 1].

Upon comparing tissue and serum visfatin levels among patient and control groups with and without dyslipidemia, there was no statistically significant difference between them ( $P = 0.498, 0.423, 0.283, \text{ and } 0.178$ , respectively). In addition, there was no significant difference with respect to metabolic

**Table 1: Comparisons between patients versus controls regarding different demographic, clinical, anthropometric data, and visfatin levels**

Point of comparison	Group						P
	Patients			Control			
	Mean±SD	Minimum	Maximum	Mean±SD	Minimum	Maximum	
Age (years)	19.53±4.21	16.00	33.00	19.83±2.25	16.00	25.00	0.732
Duration (month)	22.53±17.15	3.00	60.00				-
BMI	25.34±6.14	18.26	42.67	23.42±2.70	19.38	29.98	0.124
WC	88.43±11.55	70.00	115.00	81.97±7.63	64.00	100.00	0.014*
SBP	115.50±12.83	92.00	142.00	116.90±9.10	90.00	128.00	0.628
DBP	76.37±9.93	53.00	90.00	77.10±7.19	60.00	88.00	0.744
FPG	86.67±6.66	72.00	101.00	89.00±7.90	73.00	104.00	0.221
Cholesterol	160.07±26.22	106.00	201.00	160.50±33.12	89.00	217.00	0.955
TG	95.43±37.42	46.00	197.00	110.70±25.99	56.00	167.00	0.072
LDL	100.14±22.18	56.00	147.00	102.77±23.57	63.00	162.00	0.658
HDL	43.97±9.43	31.00	70.00	42.87±6.32	33.00	56.00	0.598
T Vis (ng/mL)	4.83±1.05	2.70	6.60	3.73±0.88	1.40	5.00	<0.001*
S Vis (ng/mL)	3.67±1.45	0.90	6.20	2.77±1.02	1.10	5.40	0.011*

SD: Standard deviation, BMI: Body mass index, WC: Waist circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FPG: Fasting plasma glucose, TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, T Vis: Tissue visfatin, S Vis: Serum visfatin. \* $P \leq 0.05$  is statistically significant

syndrome ( $P = 0.220$  and  $0.328$ , respectively). However, serum visfatin levels were significantly higher in obese/overweight group ( $P = 0.05$ ). Comparing tissue and serum visfatin in patients with moderate versus severe acne scores showed no statistically significant difference ( $P = 0.268$  and  $0.800$ , respectively) in the two groups [Table 2].

Correlations of visfatin levels in both serum and tissue with patients' demographic, anthropometric, and clinical and laboratory data showed no statistically significant values. In addition, there was no correlation between tissue and serum visfatin in both patient ( $P = 0.255$ ) ( $r = 0.214$ ) and control groups ( $P = 0.134$ ) ( $r = 0.280$ ).

**Discussion**

This study showed significantly higher tissue and serum visfatin levels in acne patients compared with controls. In agreement with our findings, Kovács *et al.* detected visfatin expression in acne skin.<sup>11</sup> We were unable to find previous reports comparing visfatin levels in tissue and serum of acne patients versus healthy controls.

Visfatin could be involved in acne pathogenesis at multiple checkpoints. First, visfatin binds insulin receptors creating insulin resistance<sup>17</sup> which stimulates duct hyperkeratinization, as in patients with Polycystic ovary syndrome (PCOS).<sup>18-20</sup> Second, visfatin stimulates proinflammatory cytokines tumor necrosis factor-alpha (TNF- $\alpha$ )<sup>21-22</sup> and interleukin-16 (IL-6).<sup>10</sup> Third, visfatin expression is increased in response to TLR-2 and TLR-4 activators connecting it to innate theory of acne.<sup>11</sup>

This study did not show a significant difference in visfatin levels (tissue and serum) between patients and controls with metabolic syndrome or dyslipidemia, a finding similar to the results of many previous studies.<sup>23-26</sup> but contradictory to the previous findings of Zhong *et al.* and Chang *et al.*<sup>27,28</sup> However, serum visfatin was significantly higher in overweight candidates.

Our study did not show significant correlation between anthropometric data and visfatin levels (both tissue and serum), similar to the results reported by Hosseinzadeh-Attar *et al.*<sup>26</sup> In our study, the waist circumference in patients was significantly higher than controls, in agreement with Del Prete *et al.*<sup>18</sup>

Comparison between visfatin levels in different acne severities showed no statistically significant difference, whereas in other diseases such as psoriasis, visfatin levels have been found to positively correlate with disease severity.<sup>8</sup>

This study showed higher tissue visfatin in acne patients, which validates a proposal by Kovács *et al.*<sup>11</sup> that visfatin expression in acne patients is due to secretion by sebocytes.

The limitation of this study was the small sample size and the need for localization of the exact cellular expression of tissue visfatin. In addition, PCOS was not evaluated in female patients.

**Conclusion**

Tissue visfatin is an important proinflammatory adipokine with significantly higher expression in acne patients.

**Compliance with ethical standards**

- All procedures performed in this study were in accordance with the ethical standards of the institutional and/or National Research Committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards
- Informed consent was obtained from all individual participants included in the study.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names

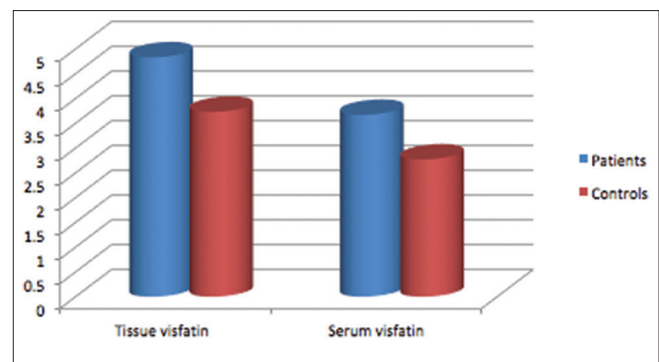


Figure 1: Comparison of visfatin levels among study groups

**Table 2: Comparison of tissue and serum visfatin in patients with moderate versus severe acne scores**

Acne score definition according to GEA scale (Dreno <i>et al.</i> , 2011)	Value	T Vis (ng/mL)	S Vis (ng/mL)
Severe: 19 (63.3%) Entire face is involved, covered with many papules and pustules, open or closed comedones, and rare nodules.	Mean±SD	4.65±1.13	3.63±1.50
	Minimum	2.70	1.00
	Maximum	6.50	6.20
Moderate: 11 (36.7%) More than half of the face is involved. Many papules and pustules, many open or closed comedones. One nodule may be present.	Mean±SD	5.15±0.85	3.74±1.44
	Minimum	3.45	0.90
	Maximum	6.60	5.70
		0.268	0.800

T Vis: Tissue visfatin, S Vis: Serum visfatin, SD: Standard deviation, GEA: Global Evaluation Acne. \* $P < 0.05$  is statistically significant

and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

#### Acknowledgement

The authors thank Dr. Mohamed AlAshry for his help in statistical analysis.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

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