A study of visfatin serum level in patients with Systemic Lupus Erythematosus (SLE)

Mekky Abd El-Monem Aly1, Mohamed Farouk Mosa1, Hatem Galal Abd Allah2 and Abd Allah Hamdy Mohammed Abozeid1

1Departments of Clinical Pathology and 2Rheumatology, Al-Hussein University Hospital, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.
Email: ahbsnakeman2015@gmail.com

Abstract: Background: Systemic Lupus Erythematosus (SLE) (also, known as Lupus) is a chronic inflammatory autoimmune disease. Visfatin is an adipokine which is secreted mainly from white adipose tissue (WAT) and is a pre B cell colony enhancing factor (PBEF) that regulates immunity and inflammation. So, it can trigger many autoimmune and inflammatory processes thus may affect SLE disease course and prognosis. Objective: Measurement of serum visfatin level in Lupus patients and healthy persons to assess its possible role in SLE. Subjects and methods: This study included 30 patients with SLE and 30 healthy volunteers with matched age and sex. So, we had two groups, patient and control. We assessed serum visfatin level in both groups by enzyme linked immunosorbent assay (ELISA). Results: As regard serum visfatin level, there was a highly statistical significant difference between control and patient groups. Results also showed a highly statistical significant positive correlation between visfatin and erythrocyte sedimentation rate (ESR) as well as C reactive protein (CRP) in patient group. Conclusion: All Lupus patients recorded high concentration of circulating visfatin and the more the ESR and CRP, the more would be the serum visfatin concentration. So, visfatin might have an important role in both inflammatory and immune processes involved in SLE. Hence, this indicates its possible role in SLE progression. Recommendation: More studies are needed to investigate this adipocytokine and its role in systemic inflammatory and immune processes in SLE. Also, more studies are required on large number of patients. Further studies could be valuable about visfatin inhibitors which might have a role in the prevention of SLE progression and complications.


Key words: SLE, Adipokines, Visfatin.

1. Introduction

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory multisystem disease mainly affecting women of child bearing age (1).

It is an autoimmune disease characterized by B cell hyperactivity, a high level of autoantibody production, immune-complex deposition and multiple organs damage (2). The accumulation of self-antigens due to impaired clearance facilitates autoimmune response and inflammation (3).

Adipose tissue forms an endocrine organ that regulates immune process and inflammation by secreting bioactive mediators called adipokines. Adipokines have been reported to play important roles in the pathogenesis of autoimmune and inflammatory diseases (4).

The term ‘adipokine’ is generally applied to biologically active substances found in the adipocytes of White Adipose Tissue (WAT); however, these factors are synthesized at other sites and participate in functions unrelated to those within WAT (5). There has been much effort to define the role of adipokines in the interaction between adipose tissue, inflammation and immunity (6).

Visfatin is an adipocytokine secreted from visceral adipose tissue, neutrophils as well as macrophages and it was initially called pre-B-cell colony enhancing factor (PBEF) that stimulates the differentiation of B-cell precursors (7). Its synthesis is controlled by several factors including glucocorticoids, tumor necrosis factor (TNF), interleukin 6 (IL-6) and growth hormone and it has been demonstrated to exert multiple pro-inflammatory functions (8). Visfatin is elevated in the systemic circulation of patients suffering from both acute and chronic inflammatory diseases (9).

Patients with inflammatory bowel disease (IBD) were found to have elevated circulating visfatin level and increased level of visfatin messenger ribonucleic acid (mRNA) in their intestinal epithelium (10).
In addition, circulating visfatin is higher in patients with rheumatoid arthritis (RA) than in healthy controls \(^{(11)}\) and its serum level was positively correlated with disease activity in RA \(^{(12)}\).

Moreover, osteoarthritis (OA) patients had higher synovial fluid (SF) visfatin concentration compared to controls that increased with OA severity. SF visfatin was positively correlated with degradation biomarker of aggrecan and collagen II suggesting its involvement in cartilage matrix degradation \(^{(13)}\).

The aim of this cross sectional case control study was to measure serum visfatin level in Lupus patients and healthy controls to assess the possible role of visfatin in inflammatory and immune processes involved in SLE.

2. Subjects and Methods

This study was a cross sectional case control study and was approved by the Research Ethical Committee. Oral and written consents were obtained from all patients and controls after a full explanation of the study. It was the result of cooperation between the Clinical Pathology and Rheumatology departments at Al-Azhar University Hospitals, Faculty of medicine.

This study included sixty (60) subjects with their ages ranging between 20-55 years. Subjects were classified into:

1. Control group: included 30 apparently healthy individuals (not affected by any comorbidity and not treated with any medications at the time of study recruitment) with matched age and sex.
2. Patient group: included 30 SLE patients which were recruited from Rheumatology and Rehabilitation department at Sayed Galal University Hospital during the period of 10th January till 20\(^{th}\) June, 2019.

Inclusion criteria:

1. SLE patients were fulfilling the American College of Rheumatology revised criteria (ACR) \(^{(14)}\).
2. Both sexes had been included especially women of child bearing age as Lupus mainly affecting women of this age \(^{(15)}\).

Exclusion criteria:

1. Age < 20 years and > 55 years old.
2. Patients with medical conditions associated with increased visfatin expression had been excluded from this study such as hypoxia, hyperglycemia, chronic kidney disease (CKD), pregnancy, labor, cancer and poly cystic ovary syndrome (PCOS) \(^{(15)}\).

All patients were subjected to Full History, clinical examination, laboratory investigations as complete blood picture (CBC), ESR, CRP, kidney and liver function tests, anti-nuclear antibodies (ANA), anti-double stranded DNA (Anti ds DNA) antibodies. In both control and patient groups, 2 ml of venous blood were taken in plain tube and left to clot at room temperature for 20 minutes then centrifuged and the serum was separated and stored at \((-20\, ^\circ C)\) until assessed for visfatin using enzyme linked immunosorbent assay (ELISA), commercial kits Catalogue No. E0025Hu; Shanghai Korain Biotech Co., Ltd.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as number and percentage.

The following tests were done:

- Independent-samples t-test of significance: was used when comparing between two means.
- Chi-square test: was used when comparing between non-parametric data.
- Pearson’s correlation coefficient (r) test: was used for correlating data.

Probability (P-value): P-value < 0.05 was considered significant, P-value < 0.001 was considered as highly significant and P-value > 0.05 was considered insignificant.

3. Results

Patients’ demographic characteristics:

Based on the inclusion and exclusion criteria, 60 patients were enrolled in the current study. Of them, 30 healthy volunteers were enrolled in the control group, whereas 30 patients were enrolled in the patient group. There were an equal proportion of females (90%) among the control and patient groups. The mean age of the included participants were 38.21±5.90 years among the patient group and 37.68±4.98 years among the patient group (p>0.05).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n=30)</th>
<th>Patients (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visfatin (ng/ml)</td>
<td>Mean 9.17</td>
<td>103.49</td>
<td>&lt; 0.001 (HS)</td>
</tr>
<tr>
<td></td>
<td>±SD 4.05</td>
<td>19.61</td>
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</tbody>
</table>

The results of this study showed:

1. Highly statistical significant difference (p < 0.001) between controls and SLE patients as regard serum visfatin (Table 1).
2. Highly statistical significant positive correlation (p < 0.001) between visfatin and ESR as well as CRP in patient group (Table 2).
3. No statistical significant difference or correlation with other demographic, clinical and laboratory data present in this study.

By T test, Table 1 showed a highly statistical significant difference between controls and patients as regard serum visfatin (mean of serum visfatin in patients and controls were 103.49 ± 19.6 ng/ml and 9.17± 4.05 ng/ml respectively, p < 0.001).

### Table (2): Correlation study between serum visfatin and ESR as well as CRP in patient group.

<table>
<thead>
<tr>
<th>Group Variables</th>
<th>Patient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visfatin vs. ESR</td>
<td>0.7</td>
<td>&lt;0.001 (HS)</td>
</tr>
<tr>
<td>Visfatin vs. CRP</td>
<td>0.81</td>
<td>&lt;0.001 (HS)</td>
</tr>
</tbody>
</table>

ESR: erythrocyte sedimentation rate, CRP: C reactive protein, r: Pearson correlation coefficient, p-value: probability value, vs.: versus

By Pearson's correlation coefficient (r) test this table showed a highly statistical significant positive correlation (p value < 0.001) between visfatin level and ESR as well as CRP (r = 0.7 and 0.81, respectively).

### 4. Discussion

All Lupus patients recorded high concentration of circulating visfatin when compared with the controls. In SLE group of patients; the more the ESR and CRP levels the more would be the serum visfatin concentration.

Systemic inflammation has been shown to modulate adipocyte metabolism and consequently adipokines levels (16).

Adipose tissue is an endocrine organ secretes hormones called adipocytokines as leptin, visfatin, resistin, apelin, omentin, sex steroids and various growth factors. So, it is regarded as a part of the endocrine system. These hormones also play an important role in the immune system (17).

In addition to adipocytokines, adipose tissue secretes inflammatory cytokines: interleukin 1(IL-1), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) that trigger many autoimmune inflammatory processes and may affect SLE disease course and prognosis (18).

Visfatin is a proinflammatory cytokine (19) and it is one of the adipocytokines that is secreted in excess from adipose tissue in obese individuals and it has numerous metabolic and autoimmune implications: it stimulates the secretion of IL-6, IL-8, IL-10, IL-18 and TNF-α. In SLE patients these may influence disease activity and delays remission (20).

The physiological role of visfatin in inflammatory diseases might involve modulation of the inflammatory or immune responses as visfatin induces chemotaxis and increases the production of IL-1, TNF, IL-6 and costimulatory molecules by cluster of differentiation 14 positive (CD14+) monocytes. This increases their ability to induce all proliferative responses (21). Hence, studies have indicated that visfatin activates human leukocytes and stimulates the production of pro inflammatory cytokines (22).

The results of this study showed that there was a highly statistical significant difference (p < 0.001) between controls and SLE patients regard serum visfatin (Table 1). This suggested that visfatin may play a major role in the regulation of the inflammatory process in SLE.

This was in agreement with Fouda et al., in 2012(23) who carried out a study to assess serum visfatin level in SLE patients and its correlation to disease activity and lupus nephritis in these patients. The study was enrolled 40 SLE patients and 40 age and sex matched healthy controls. The serum concentration of visfatin was measured with the use of ELISA method. A significantly higher serum visfatin level was found on comparing SLE patients with controls.

Also Chung et al., in 2009(24) tested the hypothesis that concentration of adipocytokines was altered in SLE. Concentration of visfatin was measured in 109 SLE patients and in 78 control persons. Concentration of visfatin (7.5 ± 10.5 vs. 4.5 ± 2.8 ng/mL, p<0.001) was higher in patients with SLE than controls.
On the other hand, Ozgen et al., in 2011\(^{25}\) have studied serum visfatin level and its association with common carotid intima-media thickness, which is a predictor of atherosclerosis, in patients with rheumatoid arthritis (RA), SLE, systemic sclerosis (SSc) and Behçet’s disease (BD). They stated that it was higher in the RA and active BD groups but not in the SLE and SSc groups. Ozgen and his colleagues compared patients with RA, SLE, SSc and BD together not SLE patients and healthy controls as in this study.

In this study, the highly significant positive correlation between serum visfatin and ESR as well as CRP supported the role of visfatin as an inflammatory mediator. This was in agreement with Fouda et al., in 2012\(^{26}\). Also, this correlation was in accordance with Oki et al., study in 2007\(^{26}\) who reported positive correlation between serum visfatin and CRP. They concluded that the elevated concentration of visfatin could reflect systemic inflammation.

It is now clear that adipokines have multiple important roles in the body and the increasing research effort is gradually revealing the adipokine-mediated interplay between adipose tissue, metabolic disorders and inflammatory autoimmune disorders.

References

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