Circulating Resistin and Visfatin Levels in Patients with Inflammatory Bowel Disease as Predictors of Treatment Response

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INTRODUCTION

Inflammatory bowel disease (IBD) is inflammatory condition of small intestine and the colon. Ulcerative colitis (UC) and Crohn’s disease (CD) are the most common two forms [1,2,3].

The pathogenesis of IBD is still not clear, it is thought that it is a result of genetic predisposition or immune response of the gut to its commensal bacteria [4], also the role of lifestyle and other factors as non steroidal anti-inflammatory drugs [5], smoking [6] or recent appendectomy [7]. Recent studies have been focused on pro-inflammatory cytokines and circulating adipokine levels [8,9].

Inflammatory bowel disease (IBD) is associated with changes in fat distribution and fat mass as increasing visceral fat mass and development of white adipose tissue (WAT) [10] and subcutaneous adipose tissue [11].

Most of adipokines are formed in WAT or in immune cells play an important role in IBD pathogenesis [12,13]. Resistin is one of the cysteine-rich proteins family, it was described as adipocyte-derived mediator of hepatic insulin resistance [14], it is produced by mononuclear cells [15], and minimal amount is produced by visceral adipose tissue [16]. Resistin has pro-inflammatory properties as it induces the production of IL-6, IL-1β and TNF-α from monocyte [17,18], it is observed to be elevated in patients with IBD [19].

Visfatin is adipokine identified in visceral adipose tissue, its structure is identical to pre-B-cell colony-enhancing factor (PBEF) [20], its level is higher in obese women compared to normal weight [21], the main source of visfatin is WAT-derived macrophages and stromal vasculature [22,23]. Visfatin has pro-inflammatory properties as
induction of TNF-α, IL-6, IL-8 by peripheral mononuclear cells [24,25]. Visfatin elevation has been observed in IBD and can be attributed to be a causative factor of decreased bone mass density in IBD [26,27].

The aim of this study was to evaluate the levels of resistin and visfatin in IBD patients before and after treatment.

PATIENTS AND METHODS
Forty patients with active IBD admitted to Tropical Medicine and Internal Medicine Departments, Zagazig University Hospitals, Egypt (age range from 20 to 43 years old) were enrolled.

Activity of Crohn's disease evaluated by CD activity index score [28], while activity in UC according to Robert et al [29].

Exclusion criteria:
Hypothyroidism or hyperthyroidism
Diabetes mellitus
Adrenal failure
Hyperlipidemia
COPD
Autoimmune disease

All patients were subjected to the following:
- Full history taking.
- Thorough clinical examination.
- Complete blood picture.
- Liver function test.
- C-reactive protein (CRP).
- Erythrocyte sedimentation rate.
- Colonoscopy and biopsies for histopathology.
- Serum level of visfatin and resistin were measured by ELISA using a commercially available kit (BioVision Research Products, Mountain View, USA) And (Linco Research, St. Charles, MO, USA) respectively before induction of treatment and 3 months after treatment.
- Informed consent was obtained from all patients and the study was approved by our Institutional Review Board.

Statistical analysis:
All data were expressed as mean and standard deviation. For quantitative data (normally distributed) comparison between two groups was done using student t-test (p <0.05; significant). All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

RESULTS
Patients were matched for age, sex. Colonoscopy and biopsy divided the patients to 10 patients with CD and 25 patients with UC with follow up loss of 4 cases and one case need surgical intervention.

The mean serum levels of resistin in Crohn's disease ranged from 12.2±2 ng/ml to 9.0±4.0 (P=0.1) and the mean serum levels of visfatin in Crohn's disease ranged from 5.6±4.6 ng/ml to 3.4±4.1 ng/ml (P=0.04) before and after treatment respectively, and the mean serum levels of resistin in ulcerative colitis ranged from 11.2±2 ng/ml to 7.5±3.1 ng/ml (P=0.039) and the mean serum levels of visfatin in ulcerative colitis ranged from 3.7±1.2 to 2.5±1.1 ng/ml (P=0.004) before and after treatment respectively.
Table (1): Patients and disease characteristics

<table>
<thead>
<tr>
<th></th>
<th>CD (N= 10)</th>
<th>UC (N= 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35 ± 9</td>
<td>40 ± 4</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 ASA</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Steroid</td>
<td>7</td>
<td>24</td>
</tr>
<tr>
<td>Azathioporine</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Infliximab</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

CD, Crohn's disease; UC, Ulcerative colitis.

Table (2): Serum level of resistin and visfatin in CD before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>CD</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Resistin</td>
<td></td>
<td>12.2 ± 2 ng/ml</td>
<td>9.0 ± 4.0 ng/ml</td>
<td>0.01</td>
</tr>
<tr>
<td>S. Visfatin</td>
<td></td>
<td>5.6 ± 4.6 ng/ml</td>
<td>3.4 ± 4.1 ng/ml</td>
<td>0.04</td>
</tr>
<tr>
<td>C. reactive protein</td>
<td></td>
<td>6 ± 1.5 mg/dl</td>
<td>0.5 ± 0.4 mg/dl</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Significant decrease in serum levels of visfatin with decrease in resistin and C. reactive protein in Crohn's disease after treatment.

Table (3): Serum level of resistin and visfatin in UC before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>UC</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Resistin</td>
<td></td>
<td>11.2 ± 2 ng/ml</td>
<td>7.5 ± 3.1 ng/ml</td>
<td>0.039</td>
</tr>
<tr>
<td>S. Visfatin</td>
<td></td>
<td>3.7 ± 1.2 ng/ml</td>
<td>2.5 ± 1.1 ng/ml</td>
<td>0.004</td>
</tr>
<tr>
<td>C. reactive protein</td>
<td></td>
<td>4.5 ± 0.5 mg/dl</td>
<td>0.5 ± 0.2 mg/dl</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Significant decrease in serum levels of visfatin with decrease in resistin and C. reactive protein in ulcerative colitis after treatment.
**Figure (1):** Serum levels of visfatin and resistin in Crohn’s disease before and after treatment.

**Figure (2):** Serum levels of visfatin and resistin in Ulcerative Colitis before and after treatment.
DISCUSSION

In the current study, we measured the circulating levels of two adipocytokines in patients with active IBD before and after induction of treatment by three months, which are produced by WAT and they are closely related to chronic inflammation, a fact that may implicate them in pathogenesis and follow up of the response to medical treatment.

In our study, both resistin and visfatin have a significantly lower circulating levels after 3 months of induction of treatment of active UC and CD patients as compared with levels before treatment (P= 0.01 and P= 0.04 respectively in CD patients and P= 0.039 and P= 0.004 respectively in UC patients, these results are inconsistence with Young et al. [30] who found that visfatin serum level decreased significantly (P= 0.046) after induction therapy suggesting as a marker of successful therapy, whereas, the serum level of resistin showed no significant alteration after treatment or significant correlation with changes in CRP or clinical indices and this may be explained by shorter duration in their study 10 weeks than in this study (12w) which may give more time for obvious significant changes.

In other study, Valenkin et al. [19] found that both resistin and visfatin were increased in active disease group not in those in remission denoting the effect of treatment and the mean serum resistin and visfatin were 12.2+2 ng/ml in CD patients and 11.2+2 ng/ml in UC patients before treatment and this was not in concordance with results obtained by Kostantinos et al. [31] who showed higher levels and this could be explained by larger number of patients and the importance of value of decrease not the one time value itself.

The CRP showed significant decrease after treatment in both CD and UC patients (P<0.01 and P<0.02 respectively) and this result is matching with that of Young et al. [30] and these results of resistin, visfatin and CRP increase their importance as possible marker for treatment response and for follow up after induction treatment.

CONCLUSION

The serum levels of resistin and visfatin decreased significantly after treatment induction for IBD, so can be used as a marker for treatment.

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Conflicts of interest: The authors declare no conflict of interest.

Ethical approval: Approved.

REFERENCES


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