



## Letter to the Editor

## Serum visfatin levels in acute appendicitis

## A B S T R A C T

## Keywords:

Visfatin

Acute appendicitis

The clinical importance of the novel adipokine visfatin are still largely unknown. Our aim was to evaluate diagnostic accuracy of visfatin serum concentrations in Acute appendicitis(AA).

Total of 34 patients with preoperative AA diagnosis (18 men and 16 women, mean age  $28.8 \pm 10.9$  years) were enrolled this study. The appendix specimens were classified as normal appendix (10 patients), acute appendicitis (24 patients). The serum levels of visfatin measured Diagnostic value of the preoperative serum visfatin levels as assessed through the corresponding ROC curve was well. (area under the curve [AUC] = 0.926,  $P < .001$ ).

In this small case series, visfatin level was found to be useful marker for diagnosis of AA.

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Visfatin, also known as pre-B cell colony-enhancing factor, is a novel adipokine secreted by fat tissue and macrophages, and it is involved in the regulation of glucose homeostasis.<sup>1</sup> Increasing evidences support the participation of this adipokine in inflammatory processes.<sup>2</sup> Visfatin stimulates the expression of Interleukin-6 (IL-6) and Interleukin-8 (IL-8) in amniotic cells and prolongs neutrophil survival in clinical sepsis. Plasma visfatin values are significantly increased in rheumatoid arthritis and polycystic ovary syndrome, two pro-inflammatory states.<sup>2–4</sup>

Acute appendicitis is one of the most common abdominal emergencies. The clinical diagnosis is often difficult even for experienced surgeons, however, as evidenced by the high rate of negative explorations, which commonly reaches 20%–30%.<sup>5</sup> A delay in diagnosis of acute appendicitis (AA) is associated with increased risk of perforation and further complications. Many attempts have been made to determine ways of decreasing the negative laparotomy rate after a clinical suspicion of AA. However, despite complete clinical history, physical examination, and the usual laboratory studies, clear decision aids for detection of early AA are lacking.<sup>5</sup>

Therefore, the aim of the present study was to test the diagnostic value of preoperative visfatin level in acute appendicitis.

Between August 2008 and December 2008, a total of 34 patients underwent appendectomy with a clinical diagnosis of acute appendicitis at the General Surgery Department, Ankara Numune Training and Research Hospital (Ankara, Turkey). The study participants comprised 18 males and 16 females (mean age  $28.8 \pm 10.9$  years). The clinical diagnosis was established preoperatively by clinical history, physical examination, and laboratory tests including WBC count and neutrophil percentage. Demographic, surgical, and histopathologic variables were recorded retrospectively. Patients underwent appendectomy with the preoperative diagnosis of acute appendicitis. The appendix specimens were classified as normal appendix (group 1; 10 patients), acute

appendicitis (group 2; 24 patients). This study was approved by the medical ethics committee of the Ankara Numune Training and Research Hospital. All subjects signed consent forms.

Serum visfatin levels were measured in duplicate with a human visfatin (COOH-terminal) enzyme immunometric assay (Phoenix Pharmaceuticals, Belmont, CA), Assay sensitivity was 2 ng/mL, and interassay and intraassay CVs were 10% and 5%, respectively.

The data were expressed as mean  $\pm$  SD. Statistical analysis was carried out using SPSS 11.0 for Windows (SPSS Inc, Chicago, Ill). The differences between the serum levels of visfatin were analysed with Mann-Whitney-U test. We measured the clinical performance of WBC count using receiver operating characteristic (ROC) curves and calculated likelihood ratios for 2 cut-points with either high sensitivity or high specificity.

A  $P$  value of  $<0.05$  was considered to be statistically significant.

The serum visfatin levels were significantly higher in the group 2 compared with the group 1 ( $66.4 \pm 13.2$  versus  $41.6 \pm 11.6$  ng/mL,  $P < .001$ ).

Diagnostic value of the visfatin as assessed through the corresponding ROC curve was well. (area under the curve [AUC] = 0.926,  $P < .001$ ) (Fig. 1).

When the cut-off value of visfatin was accepted as 45.5 ng/mL, the specificity and sensitivity were 84.6% and 90.3% respectively.

The analysis of a patient with possible appendicitis can be divided into 3 parts: history, physical examination, and routine laboratory and x-ray tests. The leukocyte count is the test probably most often used to diagnose acute appendicitis. Several reports suggest that an elevated leukocyte count is usually the earliest laboratory test to indicate appendiceal inflammation, and most of the patients with acute appendicitis present with leukocytosis.<sup>6</sup> Both leukocyte count and neutrophil percentage are not specific for acute appendicitis.<sup>7</sup>

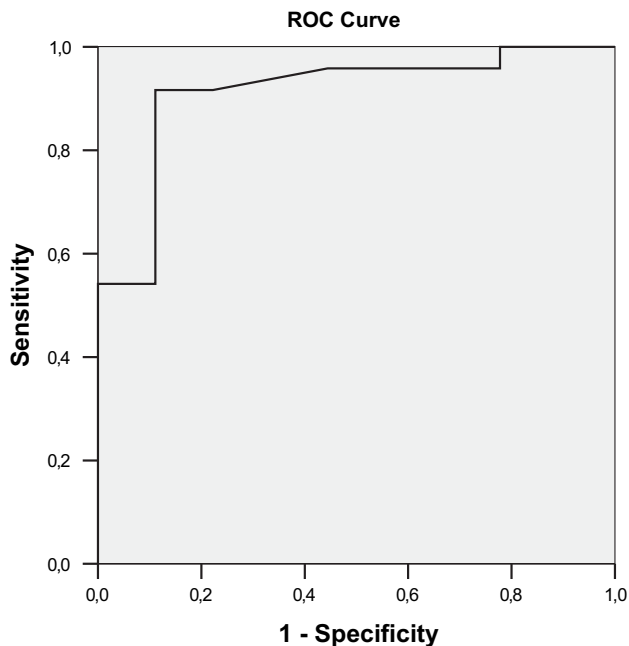


Fig. 1. Receiver operating characteristic curves of visfatin levels.

C-reactive protein is also an important serum inflammatory marker in the diagnosis of AA.<sup>8</sup> However, in a meta-analysis, CRP has been shown to have a medium sensitivity and specificity for AA.<sup>9</sup>

IL-6, IL-8, and soluble adhesion molecule CD 44 are also important inflammatory markers in the diagnosis of AA. Among these parameters IL-6 was elevated preoperatively only in gangrenous and perforated AA, and showed the best diagnostic accuracy in predicting AA.<sup>8–10</sup>

Visfatin was synthesized and released by neutrophils in response to inflammatory stimuli. Macrophages, dendritic cells, and the stromal vascular fraction contained in visceral adipose tissue expressed visfatin.<sup>2</sup> Inflammatory cytokines induced visfatin synthesis, and visfatin stimulates their expression. Recombinant visfatin was recently shown to be a potent chemotactic factor, activating human leukocytes and inducing cytokine production, especially IL-6.<sup>2</sup> Visfatin expression is up-regulated in a variety of acute and chronic inflammatory diseases including sepsis, acute lung injury, rheumatoid arthritis, inflammatory bowel disease, and myocardial infarction and plays a key role in the persistence of inflammation through its capacity to inhibit neutrophil apoptosis.<sup>11</sup>

There is an association between serum visfatin and inherent body anthropometry and cholesterol status and there is some data to suggest that cytokine estimations may change markedly in stored blood (serum over plasma) and the rapidity of storage.<sup>1,2,11</sup> These factors and visfatin gene polymorphisms may affect visfatin measurement.

In conclusion; serum visfatin level may be useful marker for diagnosis of AA but the number of subjects were limited in this study, future studies are required to confirm the results presented here.

#### Conflict of interest

There is no conflict of interest to declare.

#### Funding

None.

#### Ethical approval

This study was approved by the medical ethics committee of the Ankara Numune Training and Research Hospital.

#### References

1. Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, et al. Visfatin: a protein secreted by visceral fat that mimics the effects of insulin. *Science* 2005;**307**:426–30.
2. Bo S, Ciccone G, Baldi I, Gambino R, Mandrile C, Durazzo M, et al. Plasma visfatin concentrations after a lifestyle intervention were directly associated with inflammatory markers. *Nutr Metab Cardiovasc Dis* 2008. doi:10.1016/j.numecd.2008.09.001.
3. Otero M, Lago R, Gomez R, Lago F, Dieguez C, Gómez-Reino JJ, et al. Changes in plasma levels of fat-derived hormones adiponectin, leptin, resistin and visfatin in patients with rheumatoid arthritis. *Ann Rheum Dis* 2006;**65**:1198–201.
4. Tan BK, Chen J, Digby JE, Keay SD, Kennedy R, Randeve HS. Increased visfatin messenger ribonucleic acid and protein levels in adipose tissue and adipocytes in women with polycystic ovary syndrome: parallel increase in plasma visfatin. *J Clin Endocrinol Metab* 2006;**91**:5022–8.
5. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Laboratory tests in patients with acute appendicitis. *ANZ J Surg* 2006;**76**:71–4.
6. Keskek M, Tez M, Yoldas O, Acar A, Akgul O, Gocmen E, et al. Receiver operating characteristic analysis of leukocyte counts in operations for suspected appendicitis. *Am J Emerg Med* 2008;**26**:769–72.
7. Hallan S, Asberg A, Edna TH. Additional value of biochemical tests in suspected acute appendicitis. *Eur J Surg* 1997;**163**:533–8.
8. Peltola H, Ahlqvist J, Rapola J, Rasanen J, Louhimo I, Saarinen M. C-reactive protein compared with white blood cell count and erythrocyte sedimentation rate in the diagnosis of acute appendicitis in children. *Acta Chir Scand* 1986;**152**:55–8.
9. Hallan S, Asberg A. The accuracy of C-reactive protein in diagnosing acute appendicitis—a meta-analysis. *Scand J Clin Lab Invest* 1997;**57**:373–80.
10. Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Tröbs RB. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surg* 2006;**6**:15.
11. Luk T, Malam Z, Marshall JC. Pre-B cell colony-enhancing factor (PBEF)/visfatin: a novel mediator of innate immunity. *J Leukoc Biol* 2008;**83**:804–16.

Ferruh Kemal İşman

Department of Clinical Chemistry, Taksim Teaching and Research Hospital, İstanbul, Turkey

Barış Zülfiğaroğlu, Atahan Acar, Mahmut Koç, Mesut Tez\*  
Fifth Department of General Surgery, Ankara Numune Training and Research Hospital, Ankara, Turkey

\* Corresponding author: Fifth Department of General Surgery, Ankara Numune Training and Research Hospital, 5.cadde 10/3, Bahçelievler, 06500 Ankara, Turkey. Tel.: +90 312 508 43 02; fax: +90 312 310 34 60.

E-mail address: mesuttez@yahoo.com (M. Tez)

Mine Kücür

Department of Biochemistry, Fikret Biyal Central Research Laboratory, Cerrahpasa School of Medicine, İstanbul University, Turkey

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