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LETTER TO EDITOR

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Serum visfatin in nonalcoholic fatty liver disease

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Dear Editor:

We read with interest the study of Genc, *et al.*[1] showing similar plasma visfatin levels between men with nonalcoholic fatty liver disease (NAFLD) and healthy controls of lower body mass index (BMI) and waist circumference (WC). Furthermore, visfatin was similar in different grades of steatosis, ballooning and lobular inflammation or stages of fibrosis. Interestingly, visfatin was negatively correlated with tumor necrosis factor (TNF)-α, but not with interleukin (IL)-6, high-sensitivity C-reactive protein (hsCRP) or adiponectin.[1]

We have recently reported similar to Genc, *et al.* results regarding serum visfatin (measured with the same ELISA kit) in a Greek cohort of biopsy-proven NAFLD patients.[2] Specifically, visfatin was similar in patients with nonalcoholic steatohepatitis [NASH; 5.7 (4.2-7.7) ng/mL], simple steatosis [SS; 5.3 (4.2-6.6) ng/mL] and controls [matched for age, BMI and WC; 6.4 (3.9-7.6) ng/mL; P = 0.986].[2] Visfatin was also similar in different stages of fibrosis or grades of steatosis, ballooning, lobular and portal inflammation.[2]

Following the publication of Genc, *et al.* study,[1] we measured serum hsCRP and IL-6 and performed a *post-hoc* analysis of our own data. Serum visfatin was positively correlated with alanine transaminase (rs = 0.271; p = 0.047), total cholesterol (rs = 0.298; p = 0.028) and low-density lipoprotein-cholesterol (rs = 0.321; p = 0.018), whereas negatively with serum TNF-α levels (rs = -0.331; p = 0.033); visfatin was not correlated with total or high molecular weight adiponectin, IL-6, hsCRP, BMI, WC, insulin, homeostatic model of assessement insulin resistance or liver function tests. We also performed another post-hoc comparison: serum visfatin levels were similar in those with [n = 29; 5.4 (3.7-7.0)] and without [n = 25; 6.6 (4.6-7.7) ng/mL; p = 0.454] metabolic syndrome (MetS; IDF criteria).

Data regarding serum visfatin in histologically confirmed NAFLD patients are currently inconclusive. Jarrar, *et al.* reported similar serum visfatin between patients with NASH, SS and BMI-matched controls, although either NASH or SS had higher serum visfatin than controls of lower BMI.[3] Dahl, *et al.* reported lower serum visfatin in either SS or NASH than controls of lower BMI, but similar between SS and NASH patients.[4] Yoon, *et al.* reported similar visfatin in NASH and non-NASH patients.[5] Auguet, *et al.* reported higher serum visfatin in morbidly obese women with NAFLD than without NAFLD.[6] Available visfatin data in MetS and related morbidity remains similarly controversial. Considering the aforementioned data, it seems that BMI (or WC) is a major cofactor for visfatin levels in NAFLD patients and should be always taken into consideration in clinical studies; when groups are not matched, they should be adjusted for BMI (or WC).

Regarding specific hepatic lesions, Aller, *et al.* reported similar serum visfatin regardless the grade of steatosis, lobular inflammation and fibrosis, similarly to our and Genc, *et al.*[1] findings; on the contrary, they reported higher serum visfatin in patients with than without portal inflammation.[7] Kukla, *et al.* reported similar hepatic visfatin expression regardless the grade of steatosis, lobular and portal inflammation, but higher in patients with than without fibrosis; however, hepatic visfatin expression was similar between SS and NASH patients, as well as between patients with mild or advanced fibrosis.[8]

Despite the initial expectations for visfatin as an insulin-mimetic adipokine, more recent data showed that visfatin is mainly a proinflammatory adipokine. Visfatin induces proinflammatory cytokines, such as TNF-α and IL-6, as it was reviewed elsewhere.[9] Based on this consideration, pharmacological inhibition rather than upregulation of visfatin is under investigation for the treatment of malignant and in-

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flammatory diseases, including rheumatoid arthritis.[10] In this regard, positive rather than negative correlations between visfatin and either TNF-α or IL-6 would be expected, contrary to our and Genc, *et al*. findings.[1] Therefore, it is possible that serum visfatin, TNF-α and IL-6 levels did not reflect their hepatic levels; this may be further supported by the fact that visfatin has intracellular (enzymatic) action, beyond its extracellular (cytokine-like) action.[9] Furthermore, many other factors (diseases and medications) may affect these proinflammatory adipokines/cytokines and the drawbacks of ELISA methodology should be also taken into consideration.

In conclusion, the role of visfatin in NAFLD, if any, is currently inconclusive. It seems that serum visfatin levels cannot provide a diagnostic advantage in NAFLD patients, whereas its specific local role in adipose and hepatic tissue needs further investigation.

ABBREVIATIONS

- **BMI:** body mass index.
- **hsCRP:** high-sensitivity C-reactive protein.
- **IL:** interleukin.
- **MetS:** metabolic syndrome.
- **NAFLD:** nonalcoholic fatty liver disease.
- **NASH:** nonalcoholic steatohepatitis.
- **SS:** simple steatosis.
- **TNF:** tumor necrosis factor.
- **WC:** waist circumference.

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