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Afamin, a novel biomarker: One for all concerns?

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During the recent times, metabolic disorders are a burgeoning pandemic in nature stemming to Type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD) including dyslipidemia, hyperglycemia and insulin resistance, abdominal obesity, hypertension and clotting disorders [1]. The prevalence of metabolic syndrome is estimated at more than 30% in the United States; however, by using the Adult Treatment Panel criteria, prevalence is estimated at about 22% and increasing with age and depending on sex and ethnic origin [1,2].

Afamin, a human vitamin E binding glycoprotein which was first described in 1994 by Lichtenstein et al. as the fourth member of the human albumin gene family including albumin, a-fetoprotein, and vitamin D–binding protein, is mainly expressed in the liver and secreted into the blood stream, with molecular mass of 87000 Daltons and found on chromosome 4q11-q13 in humans [1,3].

In a three large population-based studies, i.e. from Austria, Northern Italy and Southern Germany were conducted focusing on cardiovascular and metabolic syndrome related effects phenotypes. In this study, the mean afamin concentrations were 63 ± 15, 71 ± 17 and 66 ± 14 mg/l in the Bruneck, KORA F4 and SAPHIR studies, respectively [4]. The number of metabolic syndrome components increased by 19% (incidence rate ratio [IRR]: 1.19; 95% CI:1.16–1.21; p < 0.0001) with increase of per 10 mg/l increment in afamin measured at baseline. Also, it was shown that an elevated waist circumference (OR=1.72 (95%CI 1.64- 1.80), p=5.79x10-123) at baseline and OR=1.46 (95%CI 1.31-1.63), p=2.84x10-11 for change during follow-up) and for elevated fasting glucose concentrations (OR=1.46 (95%CI 1.40-1.52), p=1.87x10-69, and OR=1.47 95%CI 1.35-1.60, p=1.01x10-18, respectively [5].

In another study, it was found that afamin concentrations were increased in patients with polycystic ovary syndrome (PCOS), then in controls (odds ratio (OR) for a 10mg/ml increase in afamin=1.3, 95% CI=1.08-1.58) [6]. Seeber, *et al.* reported that afamin concentrations were associated with the presence of metabolic syndrome in young women and serves as prognostic factor for the future development of metabolic syndrome in young women, especially those with insulin resistance and values were as PCOS with IR and PCOS without IR (73.06+/-27.36 mg/L and 64.25+/-17.41 mg/L, p = 0.033) [7].

In pregnant women the afamin concentrations were increased in two folds linearly without complications with median afamin serum concentrations of 61.9 mg/l, 79.6 mg/l, and 98.6 mg/l in the first, second, and third trimester. These further warrants investigation of the role of afamin in pregnancy related disorders [8]. Dieplinger H, *et al.* reported that, concentrations decreased from a median of 70.7 mg/L (range, 34.6-116.1 mg/L) in healthy controls to 65.2 mg/L (range, 20.2-206.6 mg/L) in patients with benign gynecologic diseases to 56.0 mg/L (range, 4.7-96.0 mg/L) in ovarian cancer patients (P < 0.001). Considering this, afamin may be an independent diagnostic marker for ovarian cancer as an adjunct marker to cancer antigen 125 (CA 125) [9].

A recently published pooled analysis has shown plasma levels of afamin strongly associated with prediabetes, diabetes mellitus related phenotype characteristics such as IR and both prevalent and incident cases of type 2 diabetes mellitus (OR 1.19 and 1.30, respectively) with afamin concentrations ranged from 61 to 73 mg/L [10].

The cohort study conducted by Kollerits B, *et al.* was first analysis conducted in >20,000 individuals as a population-based study to establish a phenotypic relationship between afamin concentration and type 2 diabetes mellitus. The main three findings were as mentioned 1) increased concentrations of afamin significantly associated with prediabetes and type 2 diabetes mellitus at baseline and other phenotypes such as insulin resistance (IR) described by HOMA-IR and whole body ISI (composite); 2) afamin concentrations were significantly predicted the development of type 2 diabetes independent from major metabolic risk factors or other parameters; 3) afamin showed a significant improvement in model fit and gain in accuracy for incident of type 2 diabetes mellitus. Afamin is primarily expressed in the liver, hence the liver plays an important role in the development of type 2 diabetes mellitus. Thus, the proposed vitamin E binding protein might be having functional relevance to the metabolic syndrome and type 2 diabetes mellitus. According to world health organization (WHO), global diabetes burden doubled since 1980s, finding crucial markers contributing to the development of type 2 diabetes mellitus and is indispensable for rapid identification of affected patients and patients at high risk [10].

In the diagnosis of metabolic disorders, clinicians are increasingly recognizing the need for prognostic biomarkers to predict future occurrence. An afamin concentration has the significant potential to predict future metabolic disorders, but it needs to be confirmed by performing large epidemiological studies including genetic association studies, animal studies and liver cell culture studies, etc. by unraveling structural and functional properties for ligand to control regulation afamin concentration.

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