



Fetuin-A in kidney disease

Marziyeh Akbari¹, Hashem Nayeri^{1*}, Hamid Nasri²

Fetuin-A is a hepatic-origin protein that secreted into the circulation (1). Fetuins had relationships with a cluster of proteins that developed from the protein cystatin through gene duplication and interchange of gene segments (2,3). Fetuin-A is a 64-kDa glycoprotein which is secreted from both adipose and hepatic tissues (4). Fetuin-A, interferes with calcification of vessels and regulation of bone metabolism in chronic kidney disease. Additionally, impaired insulin sensitivity and glucose tolerance which are features of insulin resistance have been implicated as a role of this substance. On the other hand, fetuin A significantly facilitates the integration of exogenous fatty acids into cellular triglycerides (5). Therefore, fetuin A might share a function with fatty acid binding proteins, a family of 14-kDa to 15-kDa proteins. Fetuin-A has been detected as a biomarker for neurodegenerative disease too (6). Numerous studies had detected that fetuin A inhibits ectopic calcification of the vessels (7-9). In fact, fetuin A, is exceedingly responsible for vascular calcification in overweight/obese individuals with chronic renal failure. Additionally, circulating fetuin-A is raised in obesity and the related disorders like type 2 diabetes mellitus and also metabolic syndrome (10). Elevated fetuin-A level may be related to the development of insulin resistance in diabetes and chronic renal failure and diabetic kidney disease too. Besides, serum levels of fetuin-A have been detected to have a positive association with macrovascular disease of high-risk type 2 diabetes, while no association with microvascular complications was found (11). More recently it was detected that serum fetuin-A is lower in microalbuminuric diabetic patients compared with normo-albuminuric or macroalbuminuric patients. In addition, lower serum levels of fetuin-A are linked with peripheral arterial disease in individuals with type 2 diabetes. Likewise, serum fetuin-A values are negatively correlated with atherosclerotic calcified plaques (12). However, the action of insulin on perivascular fat cells and its impact on vascular wall cells are not fully detected (13). The impact of diabetic kidney disease to increase the incidence of chronic renal failure and end-stage renal disease is enormous. Likewise, a correlation of vascular calcification and endothelial dysfunction in various

■ Implication for health policy/practice/research/medical education

Fetuin-A is a serum protein that is completely constructed by hepatic and placental cells. In hepatic and skeletal muscle cells, fetuin-A was detected to act as a natural inhibitor of insulin receptor tyrosine kinase. Recent studies detected that fetuin-A deficiency contributed to vascular calcification in chronic kidney disease and diabetes. However, exact role of fetuin-A is necessary to find in kidney health and diseases.

Keywords: Fetuin-A, Type 2 diabetes mellitus, End-stage renal disease, Hemodialysis

vascular disease have been implicated. In addition, low serum fetuin-A level may be one of the relating factors for the progress of endothelial dysfunction in chronic renal failure individuals (14). Importantly, fetuin-A was newly detected to inhibit ectopic calcification. According to this finding, fetuin-A deficiency was detected to be accompanying with calcification of vessels and increased mortality in hemodialysis patients (15). However, fetuin-A may have other functions. Recently to find the association of fetuin-A with mortality and increased risk estimate in non-dialysis chronic renal failure patients with stages of three to five, Alderson et al, conducted a study on 463 patients who recruited to the chronic renal failure standards implementation study (16). Recently, over a median follow up of 46 months, Alderson et al, could not find a clear association between fetuin-A and none of the clinical endpoints. In contrast, in an investigation, Ulutas et al, found no association of vascular calcification with fetuin-A. The study was carried out on ninety-three patients with end-stage renal disease on hemodialysis therapy (17). They concluded that diabetes mellitus and high parathormone value are more potent factors for vascular calcification in patients undergoing hemodialysis. Thus, in hemodialysis, other factors, like secondary hyperparathyroidism, hyperphosphatemia, hyperuricemia and ectopic calcification due to highly calcium × phosphate products, are potent parameters of calcification of vessel walls. A study showed in mice ablated of the fetuin-A gene, leads to myocardial

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¹Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran. ²Department of Nephrology, Isfahan University of Medical Sciences, Isfahan, Iran

*Corresponding Author: Hashem Nayeri, Email: hnaieri@gmail.com

and soft-tissue calcification (18). More recent studies showed fetuin-A deficiency has been correlated with intensification of arterial calcification and also higher mortality rates in chronic renal failure. Furthermore, Hamano et al in a cohort of chronic renal failure individuals showed that serum fetuin-A was potentially associated with coronary artery calcification (19,20). Pathologic basis of this condition is supposed to be related to derangement of insulin receptor signaling then toll-like receptor 4 activation and macrophage migration and polarization. Accordingly, adipocyte dysfunction with ensue. Hepatocyte triacylglycerol deposition and hepatic inflammation and fibrosis will detectable in the next steps. However, the major cause of mortality in hemodialysis individuals is heart and vessel complications. Thus, the exact role of fetuin-A is necessary in these patients.

Authors' contribution

MK and HN wrote the primary draft. HN edited the paper. All authors read and signed the final manuscript.

Conflicts of interest

There were no points of conflicts.

Ethical considerations

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