

## Commentary on: Is uric acid an indicator of metabolic syndrome in the first-degree relatives of patients with type 2 diabetes?

Sir,

Nowadays, metabolic syndrome is a major worldwide public health problem and is a clustering of cardiovascular risk factors like hypertension (HTN), glucose intolerance and insulin resistance.<sup>[1-5]</sup> High serum uric acid is considered to be a sign of metabolic syndrome as a result of purine metabolism disorder.<sup>[1]</sup> Recently, there has been growing evidence regarding the association between increased uric acid and metabolic syndrome.<sup>[1]</sup> Despite various prospective clinical investigations and several experimental studies that propose uric acid as a predictor of the HTN development, diabetes, and metabolic syndrome,<sup>[6-8]</sup> still an important query is, whether uric acid in the first-degree relatives of type 2 diabetes patients is an indicator of metabolic syndrome.

To find an answer, Salehidoost *et al.* conducted a study on 694 (182 male and 512 female, aged 30-69 years) first-degree relatives of type 2 diabetic patients. They found that serum uric acid was associated with waist circumference, blood pressure, tri-glyceride and HDL-cholesterol level in both sexes. In addition, the prevalence of metabolic syndrome in the fourth quartile of uric acid was significantly more than those in the first and second quartiles. They also observed a significantly higher mean of uric acid in people with metabolic syndrome compared to those without it. However; effect of uric acid in multivariate logistic regression was not significant. They concluded that, probably uric acid is not an independent factor to predict the metabolic syndrome.<sup>[9]</sup> A distinct finding of this work is that, they detected the association of serum uric with waist circumference, blood pressure, tri-glyceride and HDL-cholesterol level in both sexes in the first-degree relatives of type 2 diabetic patients. While, traditionally hyperuricemia was considered harmless except for very high concentrations (over 15 mg/dl) or for special clinical conditions such as gouty arthritis or nephropathy. Indeed, it is still debatable that uric acid is a risk factor for chronic kidney disease and cardiovascular disorders because conditions such as hypertension, hyperglycemia, and obesity are closely related to each

other and to uric acid levels. It should be noted that, uric acid is usually considered as an “innocent bystander” of deranged hemodynamic and metabolic status and not as the initiator. However, recent studies showed that elevated uric acid levels are a significant determinant for future HTN, kidney disease, cardiovascular disorders, and also mortality.<sup>[1,10,11]</sup> These findings strongly suggest that elevated concentrations of uric acid could be a causative risk factor in developing or progressing cardiovascular disorders and kidney disease.<sup>[1,10,11]</sup>

Several studies support the hypothesis entitled elevated uric acid levels might have a harmful effect, leading to endothelial dysfunction, inflammation, and vascular disease. While various clinical studies have shown that, lowering uric acid with allopurinol ameliorated endothelial dysfunction in both hyperuricemic subjects and hypertensive type 2 diabetic patients with normal uric acid levels.

The suggested mechanism is that elevated uric acid causes endothelial dysfunction by inhibiting nitric oxide synthetase, activating the renin-angiotensin system and causing pro-inflammation and resultant endothelial dysfunction, and vascular smooth muscle cell, and eventually contributing to atherothrombosis.<sup>[1,11-15]</sup> The study conducted by Salehidoost *et al.* has clinical implications, since measuring uric acid levels in the first-degree relatives of type 2 diabetic patients could uncover a group of subjects at risk. However, further clinical studies are warranted to elucidate these findings.

**Hamid Nasri**

Department of Nephrology, Division of Nephropathology, Isfahan University of Medical Sciences, Isfahan, Iran

**Address for correspondence:** Prof. Hamid Nasri,  
Department of Nephrology, Division of Nephropathology, Isfahan University of Medical Sciences, Isfahan, Iran.  
E-mail: hamidnasri@yahoo.com

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