



## Serum uric acid level and its association with cardio-metabolic risk factors in prediabetics

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Asymptomatic hyperuricemia has been detected in association with a number of situations associated with chronic renal disease, including insulin resistance, hypertension, cerebrovascular and heart disease. Experimental investigations indicate that serum uric acid may directly and indirectly promote kidney damage by various pathogenetic mechanisms both at cellular and tissue level (1,2). Recently in a cross-sectional setting, a sample containing 643 (302 prediabetic subjects and 341 normal) of the first-degree relatives of diabetic patients, the authors, found prediabetic individuals had significantly higher uric acid than normal persons (3). They also found, patients in the higher uric acid quartiles exhibited higher levels of body mass index, SBP, FBG and triglycerides. The higher quartiles of uric acid tended to be associated with higher BMI and higher total cholesterol in females prediabetic individuals. They, additionally detected, uric acid was positively associated with glucose tolerance categories. This association remained statistically significant after adjusting the effects of age and BMI. Furthermore, the association between glucose tolerance categories and uric acid were positively significant in both genders (3). They concluded that, high uric acid level was associated with some cardiometabolic risk factors in prediabetic individuals compared with normal person and also serum uric acid level was also a significant predictor for prediabetes situation (3). In recent years, much attention has been directed toward the impact of uric acid on metabolic syndrome and its role on the aggravation of kidney or hypertension. In fact, besides of various well-known risk factors such as high blood pressure and diabetes, various “non-traditional” risk factors may related to the higher risk of kidney damage compared to the general population (1-4). Recently in an investigation on 60 type II diabetics without a history of gout, we observed a significant positive correlation

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

In recent years much attention has been directed toward the impact of uric acid on metabolic syndrome and its role on the aggravation of kidney function or hypertension. It seems, in addition to the some well-known risk factors such as high blood pressure and diabetes, various “non-traditional” risk factors may related to the higher risk of kidney damage compared to the general population.

between body mass index and serum uric acid level. After adjustment for weight, a significant positive association of serum uric acid with level of proteinuria was detected too (5). Additionally, the association of serum uric acid with level of blood pressure was significantly positive (6). Accordingly, Jalalzadeh *et al.*, conducted a single-blind, randomized cross-over clinical study consisting 55 patients on regular hemodialysis with serum uric acid level >6.5 (men) and >5.5 mg/dl (women) (7-10). They noticed to the reduction of blood pressure following treatment by in their study patients (11). Recent studies shown that treatment of hyperuricemia is associated with increases of plasma 1,25(OH)<sub>2</sub>D levels, proposing that hyperuricemia may have a suppressive influence on 1- $\alpha$  hydroxylase activity (7). Hence, it is likely that, high plasma uric acid levels, reduce plasma 1,25(OH)<sub>2</sub>D levels by suppressing 1- $\alpha$  hydroxylase and, while low 1,25(OH)<sub>2</sub>D levels can stimulate parathyroid hormone. Thus, high uric acid levels may be associated with elevated PTH levels too (1-8). To attest this hypothesis, Chen *et al.*, in an in-vivo investigation on Sprague Dawley rats, found uric acid suppresses, 1 alpha hydroxylase in vitro and *in vivo* (9). In fact, a reduction in 1,25(OH)<sub>2</sub>D secondary

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to reduced 1- $\alpha$  hydroxylase enzyme activity contributes to the development of secondary hyperparathyroidism in patients with chronic kidney disease (8,9). Indeed, the direct relationship of hyperuricemia and vitamin D metabolism has two outcomes. Firstly it is well recognized that hyperuricemia by itself is an independent risk factor for renal injury in various nephropathies, like IgA nephropathy or diabetic nephropathy (8-10). Several studies, support the hypothesis that raised uric acid levels might have an injurious effect, resulting to inflammation, endothelial dysfunction and resultant vasculopathy (8-12). Secondly, regardless of the deleterious effect role of hyperuricemia on high blood pressure and worsening of some type of nephropathies, its harmful effect of vitamin D production is of significant importance (8-12). Various studies had supports, vitamin D as a negative regulator of the circulating and local tissue renin-angiotensin system (RAS), while RAS has a critical implication in the physiology of volume homeostasis and sodium and. While excess activity of RAS is associated with hypertension, renal disease and diabetes (8-12).

#### Authors' contributions

All authors contributed to the manuscript equally.

#### Conflict of interests

The authors declared no competing interests.

#### Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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