



Serum Uric acid is correlated with HbA1c levels in type 2 diabetes mellitus

Tuba Taslamacioglu Duman, Mehmet Zahid Kocak, Burcin Meryem Atak, Edip Erkus

Department of Internal Medicine, Abant Izzet Baysal University, Medical School, Bolu, Turkey

ABSTRACT

Aim: Uric acid is the product of purine metabolism and elevated serum uric acid levels are associated with many metabolic conditions. In present retrospective analysis, we aimed to compare serum uric acid levels of well controlled type 2 diabetic subjects to those of poorly controlled type 2 DM patients.

Methods: Medical database of type 2 diabetic subjects whom admitted to outpatient clinics of our institution, between January 2017 and August 2017, were retrospectively analyzed. Patients with an HbA1c level lower than 7, 5% were classified as well controlled and others were classified as poorly controlled type 2 DM group. Uric acid levels of the groups were compared.

Results: Serum uric acid level of well controlled and poorly controlled diabetics were 4.1 (2, 8-5, 9) mg/dl and 5, 9 (4-9, 6) mg/dl, respectively. The difference was statistically significant ($p < 0.001$). A Pearson's correlation test was revealed that serum uric acid was strongly and positively correlated with HbA1c ($r = 0.81$, $p < 0.001$).

Conclusion: Serum uric acid levels worsen in poorly controlled type 2 diabetic subjects. Since HbA1c levels reflects changes in 3 months period, variations in serum uric acid levels could be used as a predictor of diabetic control level in shorter time periods.

Keywords: Uric acid; HbA1c; type 2 diabetes mellitus.

Copyright © 2018 [experimentalbiomedicalresearch.com](http://www.experimentalbiomedicalresearch.com)

Corresponding Author:

Tuba Taslamacioglu Duman, M.D.

Abant Izzet Baysal University, Medical School

Department of Internal Medicine, Bolu, Turkey

E-mail: dokortuuba@gmail.com

Received 2017-12-14 Accepted 2018-01-23

Introduction

As a product of purine metabolism, uric acid, produced by the activation of xanthine oxidase enzyme. Increased uric acid, namely, hyperuricemia, is associated with hypertension [1], in oxidative stress [2], vascular smooth

muscle cell proliferation [3] and activation of white blood cells [4].

Occurrence rate of metabolic syndrome in type 2 diabetes mellitus (DM) is increased as serum uric levels elevated [5]. Moreover, hyperuricemia was found to be associated with development of chronic kidney disease in subjects with type 2 DM [6].

In present retrospective analysis, we aimed to compare serum uric acid levels of well controlled type 2 diabetic subjects to those of poorly controlled type 2 DM patients.

Methods

Medical database of type 2 diabetic subjects whom admitted to outpatient clinics of our institution between January 2017 and August in 2017 were retrospectively analyzed. Medical and laboratory data obtained from computerized database and patient file system and recorded. Patients with an HbA1c level lower than 7, 5% were classified as well controlled and others were classified as poorly controlled type 2 DM group.

Exclusion criteria were as follows: age younger than 18, active inflammation or infection, malignancy and pregnancy for women. Age, gender, height, weight, and waist circumference of the participants were obtained from computerized database and recorded.

A body mass index (BMI) was calculated by dividing of the weight in kilograms to the square of height in meters. Duration of DM was also recorded.

Serum urea, creatinine, fasting plasma glucose, uric acid, HDL cholesterol and triglyceride were obtained from the same database and recorded.

Data were analyzed by SPSS software. (SPSS 15.0; IBM Inc., Chicago, IL, USA). Kolmogorov-Smirnov test conducted to observe distribution of variables in study groups. Homogenous variables were expressed as mean \pm standard deviation and compared by independent samples t test, whereas, non-homogenous variables were expressed as median (minimum – maximum) and compared by Mann-Whitney U test. Comparison of categorical variables in study groups was conducted with Chi-square test. Correlation between studies parameters was done with Pearson's correlation analyze test. A p value of < 0.05 is considered as statistically significant.

Results

Study population was consisted of 136 subjects; 61 well controlled and 75 poorly diabetics. The patients with well-controlled type 2 DM (61 ± 12 years) were significantly older than poorly-controlled subjects (56 ± 10 years), ($p=0.02$). 36 of 61 in well-controlled type 2 DM group and 34 of 71 in poorly controlled group were women. Gender was not statistically different between study groups ($p=0.11$).

Despite well-controlled subjects were shorter (160cm [145-181]) than poorly controlled (165cm [146-178]) diabetics ($p=0.046$), weight ($p=0.21$), waist circumference ($p=0.91$) and body mass index ($p=0.79$) were not statistically different between study groups.

As expected, fasting plasma glucose of well-controlled type 2 diabetic patients (131 ± 26 mg/dl) was significantly lower than poorly controlled subjects (225 ± 19 mg/dl), ($p < 0.001$). Similarly, HbA1c of well-controlled type 2 diabetic patients (6,8% [5,1-7,4]) was significantly lower than poorly controlled diabetics (9,3% [7,6-16,5]), ($p < 0.001$).

Systolic ($p=0.74$) and diastolic ($p=0.34$) blood pressures were similar in well-controlled and poorly controlled diabetics. Serum triglyceride of well-controlled group (152 ± 55 mg/dl) was significantly lower than poorly controlled group (221 ± 74 mg/dl), ($p=0.003$). On the other hand, serum HDL cholesterol levels of the well-controlled and poorly controlled subjects were not different ($p=0.51$).

Duration of diabetes mellitus (3 years [1-20] in well-controlled vs 5 years [1-24] in poorly controlled group), blood urea (30 mg/dl [13-58] in well-controlled vs 32 mg/dl [17-58] in poorly controlled group), and creatinine (0,77 mg/dl [0,66-1,5] in well-controlled vs 0,84 mg/dl [0,5-1,87] in poorly controlled group)

was not statistically different between study groups ($p > 0.005$ for all).

Serum uric acid level of well controlled and poorly controlled diabetics were 4.1 (2,8-5,9) mg/dl and 5,9 (4-9,6) mg/dl, respectively. The difference was statistically significant ($p < 0.001$).

A Pearson's correlation test was revealed that serum uric acid was strongly and positively correlated with HbA1c ($r = 0.81$, $p < 0.001$).

Discussion

We showed in present retrospective study that serum uric acid levels are increased in poorly controlled type 2 DM patients compared to well-controlled type 2 diabetic subjects. Positive and strong correlation between uric acid and HbA1c is another important finding of our report.

Elevated serum uric acid level is a common feature in type 2 DM. Association between arterial stiffness and serum uric acid in male type 2 diabetic subjects in a study from China [7]. Another study pointed that increase in serum uric acid was related with worsening of diabetic retinopathy [8]. Similarly, increased uric acid may contribute to diabetic nephropathy. Hyperuricemia induces macrophages in renal tissue and promotes and progression of diabetic nephropathy in subjects with type 2 DM [9]. Both of these macro-vascular and micro-vascular complications of type 2 DM are associated with worse HbA1c levels. Thus, correlation between uric acid and HbA1c is not surprising.

Uric acid secretion from adipose tissue in obese is increased [10]. Authors found that uric acid levels of non-diabetic obese are higher than non-diabetic overweight subjects [11]. A report from China studied the association between serum uric acid and obesity in university students and found a positive

correlation between body mass index and uric acid [12]. Although obesity and serum uric acid levels seem to be associated in non-diabetic population, there was no relation between uric acid and body mass index, weight or waist circumference in our study.

Xue et al. compared serum uric acid levels of pre-diabetic patients and subjects with normal glucose tolerance and reported higher uric acid in pre-diabetic subjects [13].

In contrast to present report, Cui et al found that serum uric acid was negatively correlated with HbA1c levels [14]. However, authors concluded that such negative association was a result of hyperinsulinemia in type 2 DM patients. In a study from Iran, reported that pre-diabetic persons have higher serum uric acid levels compared to subjects with normal glucose tolerance [15]. However, subjects with pre-diabetes were older and more obese than normal persons in their study. Therefore, our results by comparison of uric acid levels in BMI identic groups were more valuable.

Limitations of present study are relatively small study population and retrospective design, which could make our results controversial. However, strong and positive correlation between HbA1c and serum uric acid levels is an important finding which may add a lot to current literature.

In conclusion, serum uric acid levels worsen in poorly controlled type 2 diabetic subjects. Since HbA1c levels reflects changes in 3 months period, variations in serum uric acid levels could be used as a predictor of diabetic control level in shorter time periods.

Compliance with ethical statements

Conflicts of Interest: None.

References

- [1] Mellen PB, Bleyer AJ, Erlinger TP, Evans GW, Nieto FJ, Wagenknecht LE, et al.

- Serum uric acid predicts incident hypertension in a biethnic cohort. *Hypertension*. 2006;48(6):1037-42.
- [2] Bagnati M, Perugini C, Cristiana C, Bordone R, Albano E, Bellomo G. When and why a water-soluble antioxidant becomes pro-oxidant during copper-induced low-density lipoprotein oxidation: a study using uric acid. *Biochem J*. 1999;340(1):143-52.
- [3] Rao GN, Corson MA, Berk BC. Uric acid stimulates vascular smooth muscle cell proliferation by increasing platelet-derived growth factor A-chain expression. *J Biol Chem*. 1991;266(13):8604-08.
- [4] Kanellis J, Watanabe S, Li JH, Kang DH, Li P, Nakagawa T, et al. Uric acid stimulates monocyte chemoattractant protein-1 production in vascular smooth muscle cells via mitogen-activated protein kinase and cyclooxygenase-2. *Hypertension*. 2003;41(6):1287-93.
- [5] Bonakdaran S, Kharaqani B. Association of serum uric acid and metabolic syndrome in type 2 diabetes. *Curr Diabetes Rev*. 2014;10(2):113-17.
- [6] De Cosmo S, Viazzi F, Pacilli A, Giorda C, Ceriello A, Gentile S, et al. Serum Uric Acid and Risk of CKD in Type 2 Diabetes. *Clin J Am Soc Nephrol*. 2015;10(11):1921-9.
- [7] Zhang J, Xiang G, Xiang L, Sun H. Serum uric acid is associated with arterial stiffness in men with newly diagnosed type 2 diabetes mellitus. *J Endocrinol Invest*. 2014;37(5):441-47.
- [8] Lee JJ, Yang IH, Kuo HK, Chung MS, Chen YJ, Chen CH, et al. Serum uric acid concentration is associated with worsening in severity of diabetic retinopathy among type 2 diabetic patients in Taiwan—a 3-year prospective study. *Diabetes Res Clin Pract*. 2014;106(2):366-72.
- [9] Kim SM, Lee SH, Kim YG, Kim SY, Seo JW, Choi YW, et al. Hyperuricemia-induced NLRP3 activation of macrophages contributes to the progression of diabetic nephropathy. *Am J Physiol Renal Physiol*. 2015;308(9):F993-F1003.
- [10] Tsushima Y, Nishizawa H, Tochino Y, Nakatsuji H, Sekimoto R, Nagao H, et al. Uric acid secretion from adipose tissue and its increase in obesity. *J Biol Chem*. 2013;288(38):27138-49.
- [11] Aktas G, Alcelik A, Şavlı H, Yalçın A, Öztürk S, Şit M, et al. Evaluation of Uric Acid and Gamma Glutamyl Transferase Levels in Obese and Overweight Subjects. *Bozok Medical Journal*. 2013;3(3):31-35.
- [12] Duan Y, Liang W, Zhu L, Zhang T, Wang L, Nie Z, et al. Association between serum uric acid levels and obesity among university students (China). *Nutr Hosp*. 2015;31(6):2407-11.
- [13] Xue B, Tan JB, Ning F, Sun JP, Zhang KY, Liu L, et al. Association Between Serum Uric Acid and Prevalence of Type 2 Diabetes Diagnosed using HbA1c Criteria Among Chinese Adults in Qingdao, China. *Biomed Environ Sci*. 2015;28(12):884-93.
- [14] Cui Y, Bu H, Ma X, Zhao S, Li X, Lu S. The Relation between Serum Uric Acid and HbA1c Is Dependent upon Hyperinsulinemia in Patients with Newly Diagnosed Type 2 Diabetes Mellitus. *J Diabetes Res*. 2016;2016:7184123.
- [15] Iraj B, Feizi A, Abdar-Esfahani M, Heidari-Beni M, Zare M, Amini M, Parsa F. Serum uric acid level and its association with cardiometabolic risk factors in prediabetic subjects. *J Res Med Sci*. 2014;19(3):262-67.