PROGRESS IN MEDICAL SCIENCES, 2018
VOL 2, NO. 1, PAGE 1 – 6
DOI: doi.org/10.47363/PMS/2018(2)111

ORIGINAL ARTICLE

Open Access

Significance of serum uric acid level in prediabetic and diabetic patients

Seraj Ahmed Khan[1], Saroj Mandal[2]

[1]Associate Professor, Department of Biochemistry, B.P. Koirala Institute of Health Sciences, Dharan, Nepal

[2]Technologist, Bijayapur Hospital, Dharan, Nepal

ABSTRACT

Introduction: Diabetes is a group of metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Research has shown strong links between uric acid (UA) levels and medical conditions that are related to insulin resistance, which increases the chance of acquiring diabetes, though discrepancies in result have also been reported.

Aim: This study aims to investigate the role of UA in diabetic and prediabetic subjects and compare them with euglycemic control.

Methods: In this hospital-based comparative cross-section study, 220 subjects were enrolled, out of which 76 were diabetic, 74 prediabetic, and 70 euglycemic control. The male and female ratio was almost the same in the three groups. Diabetes mellitus was defined as fasting glucose ≥126 mg/dl, non-fasting glucose ≥200 mg/dl, or use of oral hypoglycemic medication or insulin. Around 3 ml of fasting blood samples were collected and analyzed for fasting blood glucose (FBG), and UA. Two-hour post-meal blood was collected for postprandial glucose (PPG) estimation. For comparison of variables among the group's chi-square for categorical and student's *t*-test, Mann Whitney *U* and analysis of variance for continuous data were applied. Pearson's correlation coefficients were used to determine the relationships between variables. The *p*-value <0.05 was considered significant.

Results: Mean age of the diabetic, prediabetic, and euglycemic control was 56.16 ± 12.58 years, 53.69 ± 14.92 years, and 48.97 ± 14.74 years, respectively, and the difference was statistically significant (p = 0.009). The mean UA level was also statistically different in the three groups (p = 0.010), the highest level (7.50 ± 2.24 mg/dl) in diabetic patients and lowest level (6.44 ± 2.06 mg/dl) in euglycemic control. There was a positive and significant correlation between UA and FBG, PPG (r = 0.253, p =0.002; r = 0.134, p = 0.048) in the participants.

Conclusion: We observed a significant association of UA in diabetic, prediabetic, and euglycemic control; however, it is not associated with the outcome of diabetes.

ARTICLE HISTORY

Received 09 July 2018
Accepted 15 August 2018
Published 21 August 2018

KEYWORDS

Diabetic; prediabetic; uric acid; fasting blood glucose

Introduction

Serum uric acid (SUA), an end product of purine metabolism, is mainly excreted through the kidney. Hyperuricemia is probably associated with glucose intolerance due to various mechanisms. However, the most important is the association between insulin and renal resistance to absorption of urates [1]. Many chronic disorders such as hypertension [2,3], cardiovascular disease [4,5], and chronic kidney disease [6] in previous epidemiological studies have reported an association with increased SUA. Animal models have demonstrated an important role of UA in worsening insulin resistance by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake [7]. Studies have highlighted the role of elevated levels of UA as a risk factor for insulin resistance and components of the metabolic syndrome [8]. Some

Contact Seraj Ahmed Khan drserajkhan@gmail.com Associate Professor, Department of Biochemistry, B.P. Koirala Institute of Health Sciences, Dharan, Nepal.

studies reported that there is a positive association between high serum UA levels and diabetes [9–12], whereas other studies reported no association [13] or an inverse association [14].

However, the presumptive association between serum UA levels and diabetes mellitus is not clear. Moreover, the evidence from prospective studies regarding the association between UA and diabetes risk is limited. Therefore, in this study, we aimed to examine the association between serum UA and diabetic patients.

Materials and Methods

Study design and setting

This was a hospital-based comparative cross-sectional study, conducted in the Immunoassay Lab of B.P. Koirala Institute of Health Sciences. Purposive sampling technique was used.

Ethical consideration

The study was approved by Institutional Review Committee, B.P. Koirala Institute of Health Sciences, Dharan, Nepal.

Participants and sample

A total of 220 subjects were enrolled in the study. The short-preformed questionnaire was filled through the interview. Around 3 ml of blood sample was collected from the subjects. Serum was separated by centrifuging at 3,000 rpm for 10 minutes and was utilized for glucose and UA estimation.

Definition and criteria

Diagnosis of diabetes and prediabetes was made as per WHO criteria. Fasting blood glucose (FBG) of ≥126 mg/dl and postprandial glucose (PPG) of >200 mg/dl were considered as diabetes. FBG of 100–125 mg/dl and PPG of 140–199 mg/dl were considered as prediabetes. FPG of <100 mg/dl was considered as euglycemic. The cutoff level of UA for hyperuricemia in male and female was 7 and 6 mg/dl, respectively.

Analysis of parameters

Uric acid

It was estimated by the Uricase-Peroxidase method. It is based on the principle that uricase converts UA into allantoin and hydrogen peroxide. Peroxidase releases nascent oxygen from hydrogen peroxide which oxidizes a phenolic chromogen to a red color compound. The red color represents the amount of UA present in the serum and is measured at 510 nm.

Serum glucose

Glucose was estimated by Hexokinase method, which is based on the reduction of Nicotinamide Adenine Dinucleotide (NAD+) through a coupled reaction with glucose-6-phosphate dehydrogenase, and is determined spectrophotometrically by measuring the increase in absorbance at 340 nm.

Statistical analysis

The values were expressed as mean ± standard deviation, the median and interquartile range for continuous variables and number and percentage for nominal variables. Normality of the data was tested by the Kolmogorov–Smirnov test. For comparison of the data, independent *t*-test, Mann Whitney *U* test, and one-way analysis of variance (ANOVA) was used. Pearson's correlation coefficients were used to determine the relationships between variables. The analysis was done by using SPSS 11.5 version (SPSS Inc, Chicago, IL, 2002). p value <0.05 was considered as statistically significant.

Result

The total participants included were 220, out of which 76 were diabetic, 74 prediabetic, and 70 euglycemic control with a mean age of 56.16 ± 12.58 years, 53.69 ± 14.92 years, and 48.97 ± 14.74 years, respectively. There was almost equal number of male (49.5%) and female (50.5%) participants. Majority of the participants were of Janjati group (56.4%) followed by Brahmin/Chhetri (26.4%), Newar (14.5%), and Dalit (2.7%). We observed a significant difference in body mass index (BMI) (p < 0.001), systolic blood pressure (SBP) (p = 0.009), and diastolic blood pressure (DBP) (p = 0.018) in three groups. FBG and PPG in the three groups were significantly different (p = 0.001). SUA was elevated in diabetic patients (7.50 ± 2.24 mg/dl) compared to prediabetic and euglycemic control (7.25 ± 2.15 mg/dl and 6.44 ± 2.06 mg/dl), and the difference was statistically significant (p = 0.010) (Table 1).

Based on SUA, the male and female participants were grouped into normouricemic and hyperuricemic (cutoff UA value for a male was 7 mg/dl and for a female was 6 mg/dl). We observed a significant difference in FBG (p = 0.039) and PPG (p = 0.046) in normo and hyperuricemic groups in male participants; however, no association was established in

Table 1: Basic and clinical characteristics of the participants.

Variables	Diabetic	Prediabetic	Euglycemic	*p*-Value
Mean age (Years)	56.16 ± 12.58	53.69 ± 14.92	48.97 ± 14.74	0.009*
Gender				
Male (*n*)	40	37	32	0.702**
Female (*n*)	36	37	38	
Ethnicity (*n*)				
Brahmin/Chhetri	17	13	28	
Janjati	47	43	34	NA
Newar	8	17	7	
Dalit	4	1	1	
BMI (kg/m²)	26.0 ± 3.56	23.37 ± 3.23	24.03 ± 2.78	<0.001*
SBP (mmHg)	127.89 ± 16.38	122.3 ± 18.3	119.79 ± 13.3	0.009*
DBP (mmHg)	84.14 ± 15.1	78.77 ± 11.18	79.43 ± 10.58	0.018*
FBG (mg/dl)	202.75 ± 73.91	110.78 ± 7.98	96.86 ± 10.15	0.001*
PPG (mg/dl)	336.56 ± 109.87	166.51 ± 17.66	119.79 ± 11.85	0.001*
UA (mg/dl)	7.50 ± 2.24	7.25 ± 2.15	6.44 ± 2.06	0.010*

*One way ANOVA;**Pearson's chi-square; $p < 0.05$ is set as significant.

Table 2: Characterization of glycemic and other variables in normo and hyperuricemia.

Variables	Male			Female		
	Normouricemia (≤ 7 mg/dl)	Hyperuricemia (>7 mg/dl)	*p*-value	Normouricemia (≤6 mg/dl)	Hyperuricemia (>6 mg/dl)	*p*-value
Age	55.0 ± 12.64	52 ± 14.3	0.254*	50.9 ± 14.6	53.9 ± 15.6	0.299*
BMI	24.9 ± 3.2	24.7 ± 3.5	0.767*	24.1 ± 3.4	24.2 ± 3.5	0.81*
SBP	124.5 ± 15.2	122.4 ± 15.2	0.47*	124.5 ± 18.2	122.5 ± 17.3	0.564*
DBP	80.9 ± 10.9	80.6 ± 9.7	0.865*	80.4 ± 10.5	81.3 ± 17.5	0.747*
FBG	109 (99.5,131.5)	119 (103, 161.7)	0.039**	109.5 (101.7, 150.5)	116 (102.5, 147.5)	0.874**
PPG	166 (127.8, 216)	188 (142.5, 307.3)	0.046**	169 (121.9, 254.7)	164 (127.1, 237)	0.999**

*Independent *t*-test; **Mann Whitney *U*; $p < 0.05$ is set as significant.

Table 3: Correlation of parameters with UA in study participants.

Variable	*r*-value	*p*-value
Age	0.747	0.220
BMI	0.061	0.365
SBP	0.003	0.970
DBP	0.013	0.845
Fasting glucose	0.253	0.022*
Post prandial	0.134	0.048*

*Pearson's correlation; $p < 0.05$ is set as significant.

female participants (Table 2). Table 3 demonstrates the positive correlation of FBG and PPG with UA and was statistically significant ($r = 0.253$, $p = 0.022$; $r = 0.134$, $p = 0.048$). Scatter plot for the relationship between UA and FBG, PPG is depicted in Figures 1 and 2, respectively.

Discussion

In the recent past, numerous prospective and cross-sectional studies have been carried out to explore the role of UA in diabetes mellitus. The results that were produced are not unanimous, and many conflicting results have been reported. Although the majority of the studies reported an increase in the UA level in diabetic patients [10–12], some prospective studies highlighted the role of UA as the risk factor for diabetes. In this study, we reported higher UA level in diabetic as compared to prediabetic and euglycemic control. This is in line with data published in previous studies in which hyperuricemia has been associated with diabetes mellitus [9,10,14].

Kodama et al. [12] in his meta-analysis study reported that the SUA level is positively associated with the development of type 2 diabetes regardless of various study characteristics. Framingham Heart Study provides evidence that individuals with higher serum UA, including younger adults, are at a higher future risk of type 2 diabetes independent of other known risk factors [15]. The study done by Adlija et al. showed significant elevation of urine/serum ratio of UA (USRUA) levels in patients with type 2 diabetes and reported a negative USRUA correlation with the blood glucose levels, and an effect of sex and age on the UA levels. They also observed that with advancing age, levels of UA increased in diabetic patients, and males were affected by this

trend as compared to females [16]. We too observed significantly higher glucose level in male hyperuricemic individuals, which supports the above findings. The potential explanation for this could be the high glycemic level put the kidney to early damage, thereby affecting the UA excretion.

Many theories have been put forward explaining the mechanism by which UA affects the glucose metabolism. Oxidative stress has been linked to higher UA level, leading to systemic inflammation, which plays an important role in the development of diabetes [17]. Also, the role of UA in decreasing

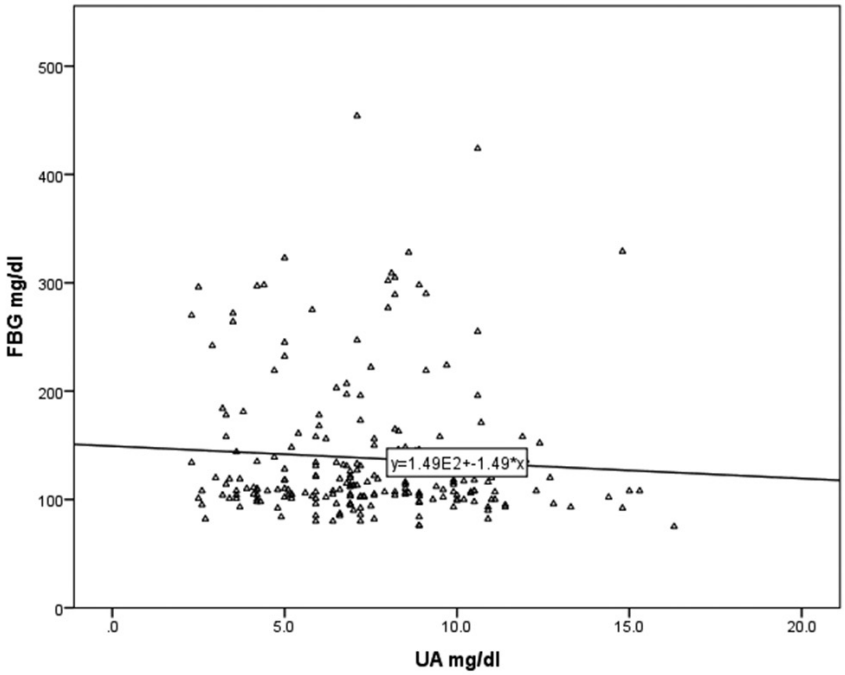

Figure 1. Scatter diagram for the relationship between UA and FPG.

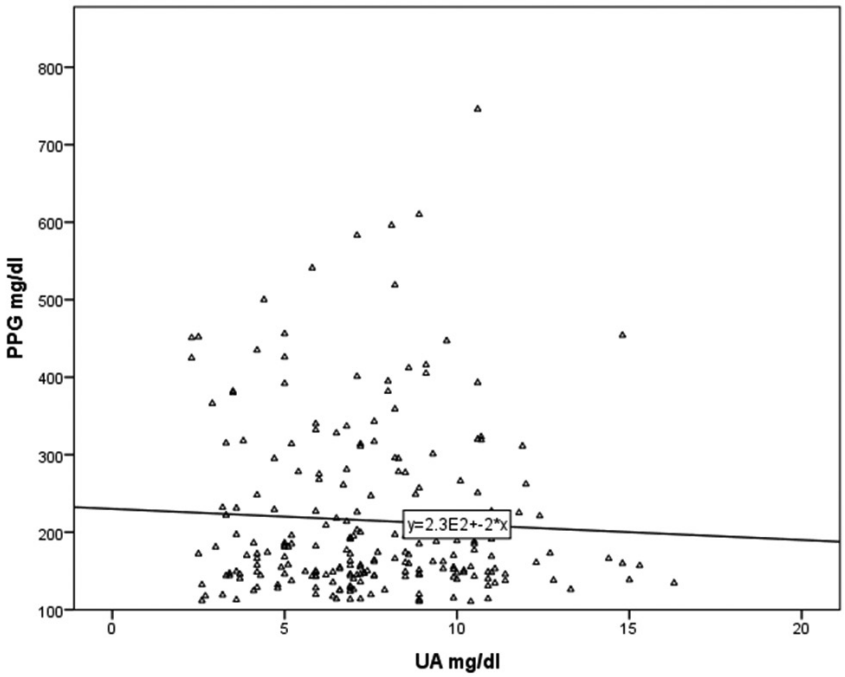

Figure 2. Scatter diagram for the relationship between UA and PPG.

endothelial nitric oxide production, thereby causing its dysfunction leading to insulin resistance, is well established [18,19]. Insulin resistance combined with high UA level may contribute to increased glucose intolerance, hypertension, and the development of diabetes.

Our results demonstrated that UA level was significantly higher in diabetic and prediabetic groups as compared to euglycemic control. There was a progressive trend, i.e., the level was highest in diabetic (7.50 ± 2.24 mg/dl) than in prediabetic (7.25 ± 2.15mg/dl) followed by euglycemic control (6.44 ± 2.06 mg/dl). This finding highlights the potential role of UA in the pathogenesis of diabetes mellitus. However, the study of glycemic variables in diabetic, prediabetic, and euglycemic control, after characterization of the male and female participants into normouricemic and hyperuricemic, shows that hyperuricemic males have higher glycemic level compared to normouricemic, which could contribute to a certain extent that UA is associated with hyperglycemia or in the progression of diabetes. However, our result does not support the study of Taniguchi et al. [13].

Conclusion

In conclusion, this study reported a significant difference in UA level in diabetic, prediabetic, and euglycemic control group. Even though we observed a positive correlation between FBG and PP with UA, but the independent association of the UA with diabetes was not significant. Therefore, further studies, especially the prospective one, are needed to explore the link between UA and diabetes and to determine whether diabetes caused the increase in UA or hyperuricemia resulted in the genesis of diabetes.

Acknowledgments

The authors would like to acknowledge the contribution of the technical staff of the Clinical Laboratory of Biochemistry Unit, B.P. Koirala Institute of Health Sciences, in helping us to perform the analysis of the parameters and also to the study participants for sharing their time and information.

Conflict of Interest

All the authors declare no any competing interest for whatsoever.

References

[1] Modan M, Halkin H, Karasik A, Lusky A. Elevated serum uric acid—a facet of hyperinsulinaemia. Diabetologia 1987; 30(9):713–8.

[2] Shankar A, Klein R, Klein BE, Nieto FJ. The association between serum uric acid level and long-term incidence of hypertension: population-based cohort study. J Hum Hypertens 2006; 20(12):937.

[3] Sundström J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. Hypertension 2005; 45(1):28–33.

[4] Klein R, Klein BE, Cornoni JC, Maready J, Cassel JC, Tyroler HA. Serum uric acid: its relationship to coronary heart disease risk factors and cardiovascular disease, Evans County, Georgia. Arch Intern Med 1973; 132(3):401–10.

[5] Fang J, Alderman MH. Serum uric acid and cardiovascular mortality: the NHANES I epidemiologic follow-up study, 1971–1992. JAMA 2000; 283(18):2404–10.

[6] Chonchol M, Shlipak MG, Katz R, Sarnak MJ, Newman AB, Siscovick DS, et al. Relationship of uric acid with progression of kidney disease. Am J Kidney Dis 2007; 50(2):239–47.

[7] Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, et al. Hyperuricemia induces endothelial dysfunction. Kidney Int 2005; 67(5):1739–42.

[8] Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ J 2005; 69(8):928–33.

[9] Dehghan A, Van Hoek M, Sijbrands EJ, Hofman A, Witteman JC. High serum uric acid as a novel risk factor for type 2 diabetes. Diabetes Care 2008; 31(2):361–2.

[10] Chien KL, Chen MF, Hsu HC, Chang WT, Su TC, Lee YT, et al. Plasma uric acid and the risk of type 2 diabetes in a Chinese community. Clin Chem 2008; 54(2):310–6.

[11] Kramer CK, Von Mühlen D, Jassal SK, Barrett-Connor E. Serum uric acid levels improve prediction of incident type 2 diabetes in individuals with impaired fasting glucose: the Rancho Bernardo Study. Diabetes Care 2009; 32(7):1272–3.

[12] Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. Association between serum uric acid and development of type 2 diabetes. Diabetes Care 2009; 32(9):1737–42.

[13] Taniguchi Y, Hayashi T, Tsumura K, Endo G, Fujii S, Okada K. Serum uric acid and the risk for hypertension and type 2 diabetes in Japanese men: The Osaka Health Survey. J Hypertens 2001; 19(7):1209–15.

[14] Oda E, Kawai R, Sukumaran V, Watanabe K. Uric acid is positively associated with metabolic syndrome but negatively associated with diabetes in Japanese men. Intern Med 2009; 48(20):1785–91.

[15] Bhole V, Choi JW, Kim SW, De Vera M, Choi H. Serum uric acid levels and the risk of type 2 diabetes: a prospective study. Am J Med 2010; 123(10):957–61.
[16] Adlija C, Sabina S, Amra MD, Bakira C, Tanza D, Maja M, et al. Relevance of uric acid in progression of diabetes mellitus. Bosn J Basic Med Sci 2010; 10(1):54–9.
[17] Johnson RJ, Kang DH, Feig D, Kivlighn S, Kanellis J, Watanabe S, et al. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension 2003; 41(6):1183–90.
[18] Sundstrom J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. Hypertension 2005; 45(1):28–33.
[19] Mellen RB, Bleyer AJ, Erlinger TP, Evans GW, Nieto FJ, Wagenknecht LE, et al. Serum uric acid predicts incident hypertension in a biethnic cohort: the Atherosclerosis Risk in Communities study. Hypertension 2006; 48(6):1037–42.