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Original Research Article

Estimation and Association of Serum Uric Acid in Type-2 Diabetes Mellitus

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Abstract

Aim: The present study aimed to know whether serum Uric acid level can be used as predictor and prognostic marker of type 2 diabetes mellitus in Patna Bihar.

Methods: The present study was conducted in the Department of Physiology. 100 patients were included in the study.

Results: Individuals in the higher uric acid quartiles were more likely to be older, overweight and obese and have high total cholesterol levels. We observed an inverse association between serum uric acid levels and diabetes mellitus in both the age- sex-adjusted and the multivariable-adjusted models. In a supplementary analysis where we examined the association between uric acid and diabetes mellitus defined in addition to fasting glucose as raised HbA1C (levels > 6.5%), compared to quartile 1 (referent) the multivariable adjusted odds ratio (95% CI) of diabetes in quartile 2 was 0.61 (0.42–0.89), quartile 3 was 0.50 (0.38–0.65), and in quartile 4 was 0.61 (0.45–0.83); P trend ≥0.004.

Conclusion: The present concluded that that higher serum uric acid levels are inversely associated with diabetes mellitus in both men and women.

Keywords: serum uric acid, type-2 diabetes mellitus, prognostic maker

Introduction

Serum uric acid, an end product of purine metabolism, has been shown to be associated with an increased risk of hypertension [1-3], cardiovascular disease [2,4], and chronic kidney disease [5] in previous epidemiological studies. Also, elevated levels of uric acid is a risk factor for peripheral arterial disease [6], insulin resistance, and components of the metabolic syndrome. [7]

Identifying risk factors for the development of type 2 diabetes is essential for its early screening and prevention. Serum uric acid (SUA) level has been suggested to be associated with risk of type 2 diabetes. Biologically, uric acid (UA) plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake. [8] However, hyperinsulinemia as a consequence of insulin resistance causes an increase in SUA concentration by both reducing renal UA secretion [9] and accumulating substrates for UA production. [10]

Diabetes mellitus type II is considered a heterogeneous disorder, it is characterized by the resistance of insulin secretory defects with varying degrees, followed by secreted reduction of insulin from the pancreas (dysfunction of pancreatic beta-cell). [11] Diabetes Type II is the wide prevalent form of diabetes, typically appearing in a person older than 40 years old, characterized by resistance of insulin and/or defect of the secretory cell of insulin. [12] Chronic diabetes is correlated with damage and failure of organs, especially the kidneys, eyes and cardiovascular system. Patients with diabetes mellitus type II are twice more likely to be anemic than non-diabetics. [13] With the progression of the illness and the development of concurrent conditions, such as cardiovascular disease (CVD), inflammation, obesity and chronic kidney disease (CKD), anemia has a passive impact on the health of diabetic patients. [14] In some cases, diabetes is associated with anemia due to its adverse effects on the organs and metabolic pathways. [15] Such iron deficiency anemia results in a reduced number of red blood cells (RBCs) due to the body does not have sufficient iron to produce them. [16] Uric acid (UA) in the blood is the final product of metabolic purine nucleotides, its excessive production and low excretion contribute to

hyperuricemia. The increases in the blood uric acid concentration can result gout and are associated with other medical conditions, such as diabetes. [17] Serum uric acid (SUA) has been linked to hypertension, cardiovascular, dyslipidemia, and renal illness in epidemiological studies. [18,19]

The present study aimed to know whether serum Uric acid level can be used as predictor and prognostic marker of type 2 diabetes mellitus in Patna Bihar.

Materials and Methods

The present study was conducted in the Department of Physiology, Patna Medical College, Patna Bihar, India for 12 months and 100 patients were included in the study.

Main Outcome of Interest

Serum glucose was measured using the modified hexokinase method at the University of Missouri, Diabetes Diagnostic Laboratory. Diabetes was defined based on the guidelines of the American Diabetes Association as a serum glucose ≥126 mg/dL after fasting for a minimum of 8 hours, a serum glucose ≥200 mg/dL for those who fasted <8 hours before their NHANES visit, or a self-reported current use of oral hypoglycemic medication or insulin.

Exposure Measurements

Age, gender, race/ethnicity, smoking status, alcohol intake (g/day), level of education, history of diabetes and oral hypo- glycemic intake or insulin administration, and antihypertensive medication use were assessed using a questionnaire. Individuals who had not smoked ≥100 cigarettes in their lifetimes were considered never smokers; those who had smoked 100 cigarettes in their lifetimes were considered former smokers if they answered negatively to the question "Do you smoke now?" and current smokers if they answered affirmatively. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Serum total cholesterol was measured enzymatically.

Rigorous procedures with quality control checks were used in blood collection, and details about these procedures are provided in the NHANES Laboratory/Medical Technologists Procedures Manual. Measurement of serum uric acid was performed by Collaborative Laboratory Services at Ottumwa, Iowa, using Beckman Synchron LX20 method. The LX20 uses a timed endpoint method to measure the concentration of uric acid in serum. Uric acid is oxidized by uricase to produce allantoin and hydrogen peroxide. The hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) and 3,5-dichloro-2-hydroxybenzene sulfonate (DCHBS) in a reaction catalyzed by peroxidase to produce a colored product. The system monitors the change in absorbance at 520 nm at a fixed time interval. The change in absorbance is directly proportional to the concentration of uric acid in the sample.

Statistical Analysis

Serum uric acid was analyzed as a categorical variable. We categorized serum uric acid level as quartiles (<4.3 mg/dL, 4.30–5.20 mg/dL, 5.30–6.20 mg/dL, >6.20 mg/dL). The odds ratio [(OR) (95% confidence interval (CI)] of diabetes mellitus for each higher uric acid quartile was calculated by taking the lowest quartile as the referent, using multivariable logistic regression models. Trends in the OR of diabetes mellitus across increasing serum uric acid category were determined by modeling uric acid categories as an ordinal variable. Sample weights that account for the unequal probabilities of selection, oversampling, and nonresponse were applied for all analyses using SUDAAN (version 8.0; Research Triangle Institute, Research Triangle Park, NC, USA) and SAS (version 9.2; SAS Institute, Cary, NC, USA) software; SEs were estimated using the Taylor series linearization method.

Results

Table 1: Characteristics of the study population by categories of serum uric acid level

Characteristics	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P value
Age, years	44.86 ± 0.32	42.68 ± 0.36	45.55 ± 0.39	48.72 ± 0.34	<0.0001
Women, %	54.46 ± 1.56	55.73 ± 1.17	48.42 ± 1.24	52.02 ± 1.14	0.0073
Education categories, %					0.0002
Below high school	23.37 ± 1.42	22.58 ± 1.15	21.70 ± 1.34	26.14 ± 1.34	
High school	33.17 ± 1.34	36.84 ± 1.18	32.48 ± 1.54	35.55 ± 0.98	
Above high school	43.50 ± 2.11	40.58 ± 1.63	45.82 ± 1.66	38.31 ± 1.38	
Smoking, %					<0.0001
Never smoker	48.06 ± 1.44	45.25 ± 1.52	49.19 ± 1.64	48.04 ± 1.31	
Former smoker	21.23 ± 1.07	23.77 ± 1.02	24.96 ± 1.19	29.21 ± 0.98	
Current smoker	30.71 ± 1.21	30.98 ± 1.62	25.85 ± 1.33	22.75 ± 1.18	
Alcohol intake, %					
Current drinker	55.35 ± 1.95	54.16 ± 1.84	56.94 ± 1.44	54.46 ± 1.82	0.0680

Body mass index, kg/m^2					<0.0001
Normal	64.86 ± 1.42	54.24 ± 1.15	39.75 ± 1.28	25.35 ± 0.88	
Overweight	27.93 ± 1.10	33.27 ± 0.89	35.34 ± 1.44	34.96 ± 1.32	
Obese	7.21 ± 0.77	12.49 ± 0.98	24.91 ± 1.11	39.69 ± 1.22	
Total cholesterol, mg/dL	194.06 ± 0.72	200.52 ± 0.74	204.06 ± 0.72	212.88 ± 0.72	<0.0001

Individuals in the higher uric acid quartiles were more likely to be older, overweight and obese and have high total cholesterol levels.

Table 2: Association between serum uric acid level and diabetes mellitus

Serum uric acid level	Age- and sex-adjusted odds ratio (95% confidence interval)	Multivariable-adjusted odds ratio (95% confidence interval)
Quartile 1 (<4.30 mg/dL)	1 (reference)	1 (reference)
Quartile 2 (4.30–5.20 mg/dL)	0.63 (0.44–0.91)	0.54 (0.36–0.80)
Quartile 3 (5.30–6.20 mg/dL)	0.62 (0.45–0.85)	0.40 (0.29–0.56)
Quartile 4 (>6.20 mg/dL)	0.54 (0.30–097)	0.48 (0.35–0.66)
P trend	0.0022	<0.0001

We observed an inverse association between serum uric acid levels and diabetes mellitus in both the age-sex-adjusted and the multivariable-adjusted models. In a supplementary analysis where we examined the association between uric acid and diabetes mellitus defined in addition to fasting glucose as raised HbA1C (levels > 6.5%), compared to quartile 1 (referent) the multivariable adjusted odds ratio (95% CI) of diabetes in quartile 2 was 0.61 (0.42–0.89), quartile 3 was 0.50 (0.38–0.65), and in quartile 4 was 0.61 (0.45–0.83); P trend ≥0.004.

Discussion

An abnormality in insulin synthesis or activity may cause diabetes mellitus (DM), a metabolic disorder that affects the metabolism of protein, carbohydrate and fat. Hyperglycemia and the excretion of urine glucose are signs of DM. [20] The link between SUA levels and blood glucose concentrations in healthy persons has been studied in just a few of research. There are several risk factors for cardiovascular disease that are linked to elevated levels of uric acid, hence it is critical to determine the exact SUA value in diabetic, prediabetic, and healthy persons. As hyperuricemia is common, it is vital to investigate its impact on a wide range of disorders. The relationship between hyperuricemia and its comorbidities has been studied extensively. [21] Both hyperuricemia and anemia share comorbidities such as chronic kidney disease and cardiovascular disease. [22]

Previous studies examining the association between serum uric acid levels and diabetes mellitus were restricted to specific racial/ethnic groups and gender and were not consistent in their findings. Some studies reported that there is a positive association between elevated serum uric acid levels and diabetes [23-25], whereas some other study reported no positive association between serum uric acid and diabetes mellitus. [26] Also, some studies reported that serum uric acid is inversely associated with diabetes mellitus. [27,28] Individuals in the higher uric acid quartiles were more likely to be older, overweight and obese and have high total cholesterol levels. We observed an inverse association between serum uric acid levels and diabetes mellitus in both the age- sex-adjusted and the multivariable-adjusted models. In a supplementary analysis where we examined the association between uric acid and diabetes mellitus defined in addition to fasting glucose as raised HbA1C (levels > 6.5%), compared to quartile 1 (referent) the multivariable adjusted odds ratio (95% CI) of diabetes in quartile 2 was 0.61 (0.42–0.89), quartile 3 was 0.50 (0.38–0.65), and in quartile 4 was 0.61 (0.45–0.83); P trend ≥0.004.

Chronic inflammation in diabetes anemic patients is connected to high C-reactive protein levels, although iron levels in diabetic and anemic patients were low, showing that ferritin increases were tied to the chronic inflammatory process. Additionally, serum ferritin was shown to be connected with BMI, glucose levels, and insulin sensitivity, all of which were positively correlated. [19] A plausible mechanism for the observed results of an inverse association between increasing serum uric acid and diabetes mellitus may be related to the inhibition of uric acid reabsorption in the proximal tubule by high glucose levels in diabetic individuals. [29,30] We found that in the current study, an inverse association was observed between elevated serum uric acid and diabetes mellitus even after adjusting for age, sex, education, smoking, alcohol intake, BMI, hypertension, and serum total cholesterol in both subgroup analysis by gender and hypertension.

Conclusion

The present concluded that that higher serum uric acid levels are inversely associated with diabetes mellitus in both men and women.

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