World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
Original Article

Serum uric acid levels and its association with type 2 diabetes mellitus

Dr Sanjeev Kumar[1], Dr Pallavi Mahajan[2], Dr Ashima Badyal[3*]

[1]Assisatnt Professor, Department of Medicine, GMC, Kathua, J&K
[2]Assistant Professor, Department of Biochemistry Acharya Shri Chander College of Medical Sciences and Hospital
[3*]Lecturer, Department of Biochemistry, GMC, Jammu, J&K

Received: 19-02-2019 / Revised Accepted: 17-03-2019 / Published: 30-03-2019

ABSTRACT

Diabetes Mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. Elevated uric acid levels are often found in individuals with the metabolic syndrome. A prospective study was conducted on 400 type 2 diabetic patients attending the Medicine OPD (Sub District Hospital Hiranagar) from July-December 2018, with the aim to find correlation between uric acid and glycemic status in type2 DM. Patients of type 2 DM were diagnosed as fasting plasma glucose ≥ 126mg/dl and 2 hrs post prandial glucose ≥ 200mg/dl. Among the male patients, 46.8% were above 60 years of age group and only 6.9% in the age of 30-39 years as compared to females having relative percentage of 44.5 & 7.1 in the respective age groups. The SUA concentration rose with increasing fasting plasma levels up to the level of 140 mg/dl, but decreased thereafter. It was observed that Uric Acid was positively related to BMI and inversely related to HbA1c, FBS and RBS. Since HbA1c, FBS and RBS are typically taken to be diagnostic criteria for T2DM, Serum Uric Acid (SUA) might act as predictor and marker of T2DM but its clinical implications need to be studied further.

Keywords: T2DM, Metabolic syndrome, Uric acid, Diabetic patients

Address for Correspondence: Dr. Ashima Badyal, 214 Av Shastri Nagar, Jammu, J&K, India: 180004; Email: badyal.ashima@gmail.com

How to Cite this Article: Dr Sanjeev Kumar, Dr Pallavi Mahajan, Dr Ashima Badyal. Serum uric acid levels and its association with type 2 diabetes mellitus. World J Pharm Sci 2019; 7(4): 38-42.

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INTRODUCTION

Diabetes is a progressive disease in which the risks of myocardial infarction, stroke, microvascular events, and mortality are all strongly associated with hyperglycemia. Diabetes is known to cause long term dysfunction of various organs like heart, kidneys, eyes, nerves and blood vessels.[1] Among the various types of diabetes, type2 is the most common form affecting approximately 90-95% of diabetics world-wide and accounts for most of the public health burden attributable to diabetes.[2] Diabetes has evolved into an epidemic in India. The estimated number of patients in India with diabetes was 62.4 million in 2011, which is protected to rise to a staggering 101.2 million by 2030.[3] In the year 2000, India topped the world with the highest number of people with diabetes mellitus (31.7 million) followed by China (20.8million) with the United States (17.7 million) in second and third respectively.[4]

Many pathogenic processes are involved in the development of diabetes. These processes range from autoimmune destruction of the cells of the pancreas with consequent insulin deficiency to abnormalities which result in resistance to action of insulin. The basis of the abnormality in carbohydrate, protein metabolism and fat in diabetes is deficient action of insulin on target tissues.[5] Deficient insulin action usually results from inadequate insulin secretion and or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action.[6] Defects in insulin action and impairment of insulin secretion frequently coexist in the same patient, and it is even often unclear which abnormality, if either alone, is the primary cause of hyperglycemia.

Symptoms of marked hyperglycemia include polydipsia, polyuria, weight loss, sometimes expressed as blurred vision and polyphagia. Susceptibility to certain infections and impairment of growth may also accompany chronic hyperglycemia. Acute, life threatening consequences of uncontrolled diabetes usually include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations and charcot joints; and autonomic neuropathy causing genitourinary, gastrointestinal, cardiovascular incidence, peripheral arterial, and Cerebrovascular disease.[7] Hypertension and abnormalities of lipoprotein metabolism are mostly common in people with diabetes. Once high risk patients are identified, those adherent to a program of 30 min of moderate physical activity per day and can get weight loss of 5-10% of initial body weight, can usually expect to reduce the risk of type 2 diabetes by at least 50% in relation to patients who are not following a therapeutic lifestyle program.

Uric acid is the end product of protein metabolism. Xanthine oxidase catalyses the oxidation of xanthine and hypoxanthine into uric acid, producing O2 and H2O2 as by-product.[8] Serum urate levels vary with age and sex. Most children usually have serum urate concentrations of 3.0-4.0 mg/dl. Levels usually begin to rise in males during teenage years but remain low down in females until menopause. Mean serum urate values of adult men and pre-menopausal women are 6.8 and 6.0 mg/dl, respectively. After menopause, values for women increase to near those of men in adulthood, concentrations rise gradually over time and differ with body weight, height, blood pressure, renal function and alcohol intake. Several epidemiological studies have reported that high serum levels of uric acid are strongly associated with prevalent health conditions such as obesity, insulin resistance, metabolic syndrome and diabetes, essential hypertension, renal disease.[9] In recent decades, serum uric acid has emerged as a potential risk factor for type 2 DM . The role of uric acid in abnormal carbohydrate metabolism is also uncertain. It is not clear whether uric acid is causative of insulin resistance or beta cell secretory deficiency, or is it a by-product of insulin resistance or hyperglycemia.[10]

This is an important question because if uric acid is cause, then lowering down high serum uric acid levels may be aim for early intervention utilizing anti-hyperuricemic agents readily available in the market. If uric acid is just a by-product of impaired glucose metabolism, it may still be useful as an early marker of T2DM risk and guide to earlier interventions, but not by treating hyperuricemia. Hyperinsulinemia has been shown to cause hyperuricemia. There are hypothesis that high uric acid is simply a by-product of insulin resistance and glucose metabolism dysfunction.[11]

However, serum uric acids are also strongly associated with prevalent health conditions such as obesity, metabolic syndrome, essential hypertension and renal disease. Hyperuricemia is an independent risk factor for cardiovascular diseases.[12] Keeping in view the above facts, the present study aims to evaluate serum uric acid levels in type 2 diabetics and understand its correlation with HbA1c, RBS and FBS levels.

MATERIALS AND METHODS

A prospective study was conducted on 400 type 2 diabetic patients attending the Medicine OPD (Sub-District Hospital, Hiranagar) within a period 6

months i.e., July 2018-December 2018. Detailed history was taken. General physical examination, detailed systemic examination and investigations were carried out. Individuals in the age group 30-70 years suffering from T2DM, of either gender were included in this study. Written informed consent was taken from the patients. Ethical approval was taken from hospital review board.

Patients known to have cardiovascular disease, cerebrovascular disease, gouts, or on taking medicines like diuretics, levodopa, pyrazinamide and or all any other condition which may increase or decrease serum uric acid levels were excluded from the study.

Patients of type 2 DM were diagnosed as fasting plasma glucose >126mg/dl and 2 hrs post prandial glucose> 200mg/dl, may be asymptomatic for many years, most of the patients being obese, gradual onset of symptoms and ketoacidosis seldom occurring. In the current study, enzymatic method was used to test the samples: glucose oxidase (GOD) converts glucose into gluconic acid; hydrogen peroxide formed in this reaction in presence of peroxide (POD) to produce red quinoneimine dye. This dye has absorbance maximum at 505nm. (500-550nm) The intensity of colour is directly proportional to the glucose in specimen.[13]

Uricase method was evaluated by clinical and laboratory standards institute in 2003,[14] defining the principle as: uric acid, which absorbs light at 293nm is converted by uricase to allantoin, which is non-absorbing at 293nm due to the appearance of uric acid, which is directly proportional to the concentration of uric acid in the sample and is measured using a bichromatic 293, 700nm; giving the reference range of uric acid : females 2.6-6.0 mg/dl; males 3.5-7.2mg/dl.

RESULTS AND DISCUSSION

The observations were presented and studied in tabulated forms under various correlations and comparisons. Among the male patients, 46.8% were above 60 years of age group, while 46.3 % were in the age group between 40 to 59 years and only 6.9% in the age of 30-39 years as compared to females having relative percentage of 44.5, 48.4 & 7.1 in the respective age groups which was very much comparable. (Table 1)

Mean values for various biochemical parameters of diabetic patients deviated from the standard mean maximums and mean minimums significantly for each parameter (FBS, RBS, SUA and HbA1c). (Table 2 & 3)

Gender-wise distribution showed the male patients with comparatively higher test values but without no significant variance with P Value remaining insignificant ($p>0.01$). (Table 4)

Correlation of parameters for age category/groups: 40-49 and 50-59, which are generally considered at high risk of T2DM, also did not show much significant variation between them. (Table 5)

Mean values of SUA with FBS, RBS and HbA1c showed an inverse relationship in general. (Tables 6, 7 & 8)

The study revealed an inverse relationship between DM and increase in Serum Uric Acid Levels. The SUA concentration rose with increasing fasting plasma levels up to the level of 140 mg/dl, but decreased further for fasting plasma levels above 140 mg/dl. Similar trend was observed for HbA1c levels. This observation was similarly made by Nan H et al (2010).[15]

In the current study, it was observed that Uric Acid was positively related to BMI and inversely related to HbA1c, FBS and RBS. All these are supported by the findings of Bandaruet al.[16] This phenomena and mechanism can be attributed to uric acid inhibition, re-absorption in the proximal tubule by high glucose levels in diabetic patients. Since HbA1c, FBS and RBS are typically taken to be diagnostic criteria for T2DM, it can be established that Serum Uric Acid Levels are having positive association with the risk of T2DM and can be recommended to be and independent predictor of the development of T2DM.

CONCLUSION

It can be easily concluded from the statistical facts generated out of this study that serum uric acid in patients of diabetes mellitus is inversely related to FBS, RBS and HbA1c levels. Serum Uric Acid (SUA) might act as predictor and marker of T2DM but its clinical implications need to be studied further.

Table 1: Distribution of diabetic patients according to their age and gender

Age Category *years*		Gender		Total
		Male	Female	
30-39	N	15	13	28
	%	6.9%	7.1%	7%
40-49	N	41	34	75
	%	18.8%	18.7%	18.7%
50-59	N	60	54	114
	%	27.5%	29.7%	28.5%
>=60	N	102	81	183
	%	46.8%	44.5%	45.8%
Total	N	218	182	400
	%	100%	100%	100%
	% out of total	54.5%	45.5%	100%

Table 2: Mean normal values for controls

Parameters	Minimum	Maximum
FBS	70 mg/dl	130 mg/dl
RBS	80 mg/dl	200 mg/dl
SUA	2.6 mg/dl	7.2 mg/dl
HbA1c	4.0%	5.6%

Table 3: Mean values for various biochemical parameters of diabetic patients

Parameters	N	Minimum	Maximum	Mean ± SD
FBS	400	108 mg/dl	219 mg/dl	141.11±13.68 mg/dl
RBS	400	180 mg/dl	435 mg/dl	255.86±29.04 mg/dl
SUA	400	2.5 mg/dl	8.7 mg/dl	4.05 ±0.68mg/dl
HbA1c	400	6%	10%	8.01±0.76%

Table 4: Gender-wise distribution of Diabetic patients for various parameters

Parameters	Sex	N	Mean ± SD	P Value
Age	M	218	57.12 ±13.12Yr	0.146
	F	182	55.56 ±12.51Yr	
FBS	M	218	143.20 ±13.84mg/dl	0.035
	F	182	140.10 ±13.53mg/dl	
RBS	M	218	256.90 ±29.63mg/dl	0.845
	F	182	253.95 ±28.82mg/dl	
SUA	M	218	4.06 ±0.89mg/dl	0.120
	F	182	4.01 ±0.87mg/dl	
HbA1c	M	218	8.4 ±0.40 %	0.474
	F	182	8.4 ±0.68 %	

Table 5: Correlation of BMI, SUA and HbA1c in age category: 40-59 Years

	Age Category	N	Mean ± SD
BMI	40-49	75	26.78 ± 3.04
	50-59	114	27.05 ± 3.41
SUA	40-49	75	4.06 ± 0.93
	50-59	114	4.01 ± 0.95
HbA1c	40-49	75	7.00 ± 0.96
	50-59	114	7.93 ± 0.89

Table 6: Mean values of SUA and FBS in diabetic patients

FBS	SUA	
mg/dl	Mean	N
100-120	3.0	2
120-140	3.98	161
>=140	3.89	237
Total		400

Table 7: Mean values of SUA and RBS in diabetic patients

RBS mg/dl	SUA	
	Mean	N
180-200	4.70	2
200-220	4.65	29
220-240	4.15	30
240-260	3.95	86
>=260	3.82	253
Total		400

Table 8: Mean values of SUA and HbA1c in diabetic patients

HbA1c	SUA	
	Mean	N
<7%	4.173	32
7-8%	4.239	84
8-9%	4.227	102
>=9%	4.164	82
Total		400

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