

Original Research

Correlation between serum uric acid and microangiopathic complications in diabetes mellitus patients

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ABSTRACT:

Background: Type 2 diabetes mellitus (T2DM) is undoubtedly one of the most challenging health problems in the 21st century and the number of diabetic patients diagnosed has reached 366 million in 2011. The present study was conducted to evaluate serum uric acid as a risk factor for micro-vascular complications of diabetes mellitus. **Materials & Methods:** The present study was conducted on 168 patients with type II diabetes mellitus of both genders. 10 ml of blood was obtained for assessment of blood glucose and uric acid level. **Results:** Age group 40-60 years had 92, 60-80 years had 50 and >80 years had 26 patients. The difference was significant ($P < 0.05$). hyperuricemia was positive in 112 and negative in 56. The difference was significant. out of 112 patients with hypertension, 84 had high and 28 had low serum uric acid level. Out of 56 patients who had not hypertension, 36 had high serum uric acid and 20 had low. The difference was significant ($P < 0.05$). Among 96 patients who had stroke, 56 had high serum uric acid and 40 had low uric acid. The difference was significant ($P < 0.05$). Serum uric acid and urine micro albumin level was elevated with duration of diabetes mellitus. **Conclusion:** Elevated serum uric acid levels in type 2 diabetes mellitus cause more micro vascular and macro vascular complications. **Key words:** Diabetes Mellitus, uric acid, vascular complications.

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INTRODUCTION

World Health Organization (WHO) defines the term Diabetes Mellitus (DM) as a metabolic disorder of multiple etiology, characterized by chronic hyperglycaemia with disturbances of carbohydrate, protein and fat metabolism, resulting from defects in insulin secretion or insulin action or both.¹ Type 2 diabetes mellitus (T2DM) is undoubtedly one of the most challenging health problems in the 21st century and the number of diabetic patients diagnosed has reached 366 million in 2011. Complications due to diabetes are a major cause of disability, reduced quality of life and death. The number of patients diagnosed each year with macrovascular and microvascular complications attributed to T2DM is rising. Cardiovascular diseases and nephropathy are the leading causes of death for people with T2DM and type 1 diabetes mellitus, respectively. Therefore, much epidemiologic evidence were committed

to risk factors related to development of T2DM and its complications.²

Serum uric acid (SUA), the product of purine metabolism, used to be thought predominantly as a predictor of gouty diathesis. However, as a member of metabolic syndrome (MetS), uric acid (UA) could worsen insulin resistance by disturbing insulin-stimulated glucose uptake. Recent studies have demonstrated that serum uric acid levels are higher in subjects with prediabetes and early type 2 diabetes than in healthy controls. Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance or hyperinsulinemia in metabolic syndrome. This study was carried out to evaluate the level of serum uric acid in type 2 Diabetes mellitus patients and to correlate the parameters of diabetic nephropathy like microalbuminuria and serum creatinine levels with uric acid in type 2 Diabetes mellitus subjects.³

The pathophysiology of chronic microvascular complications of T1D is complex, involving the interaction between genetic susceptibility, metabolic, and environmental factors. Many risk factors have already been associated with the development and progression of diabetic nephropathy, such as elevated HbA1c, duration of diabetes, presence of concomitant microvascular complications and elevated albumin excretion rate.⁴ In recent years there has been a debate regarding the association of hyperuricemia with diabetic complications. If this association is conclusively established, therapeutic interventions aiming to reduce uric acid synthesis might help to retard the progression of microvascular complications of diabetes. Hence this study was conducted

to evaluate serum uric acid as a risk factor for microvascular complications of diabetes mellitus.

MATERIALS & METHODS

The present study was conducted in the department of General Medicine, Rajshree Medical Research Institute, Bareilly, Uttar Pradesh, India. It comprised of 168 patients with type II diabetes mellitus of both genders. The study was approved from institutional ethical committee. All participants were informed regarding the study and written consent was obtained.

Data such as name, age, gender etc. was recorded. 10 ml of blood was obtained for assessment of blood glucose and uric acid level. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

RESULTS

Table 1: Age wise distribution of patients

Age group (Years)	Number	P value
40- 60	92	0.01
60-80	50	
>80	26	

Table 1 shows that age group 40-60 years had 92, 60-80 years had 50 and >80 years had 26 patients. The difference was significant (P< 0.05).

Table 2: Association between Hyperuricemia and Diabetes Mellitus

Hyperuricemia	Number	P value
Positive	112	0.01
Negative	56	

Table 2 shows that hyperuricemia was positive in 112 and negative in 56. The difference was significant (P< 0.05).

Table 3: Association between Hypertension and Serum Uric Acid Levels

Hypertension	Serum uric acid		P value
	High	Low	
Yes	84	28	0.01
No	36	20	

Table 3 shows that out of 112 patients with hypertension, 84 had high and 28 had low serum uric acid level. Out of 56 patients who had not hypertension, 36 had high serum uric acid and 20 had low. The difference was significant (P< 0.05).

Table 4: Association between the Serum Uric Acid and Cerebrovascular Accident

Stroke	Serum uric acid		P value
	High	Low	
Yes	56	40	0.01
No	40	32	

Table 4 shows that among 96 patients who had stroke, 56 had high serum uric acid and 40 had low uric acid. The difference was significant (P< 0.05).

Table 5: Association between the Serum Uric Acid and Urine Micro Albumin

Duration of diabetes	Number	Urine Micro Albumin in Diabetes Patients	Urine Micro Albumin
0-3	112	5.22	38.4
4-6	92	6.34	46.8
7-10	48	7.60	52.8
>10	24	7.54	54.6

Table 5 shows that serum uric acid and urine micro albumin level was elevated with duration of diabetes mellitus.

DISCUSSION

Over recent years there has been debate about the nature of this association between raised serum uric acid concentration and cardiovascular disease. If the association between hyperuricemia and diabetic complications is conclusively established, therapeutic interventions targeted at uric acid levels may benefit these patients.

In vitro studies show that uric acid may have antioxidant properties. SUA works as a scavenger of free radicals, reacting with a series of oxidants, especially peroxynitrite.⁵ Other studies, both in vitro and in vivo, suggest that high levels of SUA may promote endothelial dysfunction, hypertension, and metabolic syndrome by inducing oxidative stress. In fact, there is evidence that the use of drugs that lower serum uric acid can revert these conditions.⁶ The present study was conducted to evaluate serum uric acid as a risk factor for microvascular complications of diabetes mellitus.

In present study, age group 40-60 years had 92, 60-80 years had 50 and >80 years had 26 patients. Hyperuricemia was positive in 112 and negative in 56. Kodama et al⁷ found that a total of 120 cases of type 2 Diabetes mellitus, out of which there were 69 males (57.5%) and 51 females (42.5%), with a mean age of 59.04 ± 13.47 years. Mean FBS was 186.10 ± 77.53 mg/dl with majority of the subjects having elevated FBS. Mean PPBS of 274.94 ± 108.66 mg/dl and of HbA1c 8.15 ± 1.7 was observed. The uric acid of majority number of our study participant males (65.22%) had level of ≥ 7.4, with a mean of 9.53 ± 4.38. Mean blood urea and serum creatinine levels were 46.91 ± 15.13 and 1.44 ± 0.29 respectively. There was significant association seen between uric acid levels and urine albumin, serum creatinine, twenty four hour urinary albumin, FBS and PPBS levels and HbA1c levels.

Hyperinsulinemia as a consequence of insulin resistance causes an increase in serum uric acid concentration by both reducing renal uric acid secretion and accumulating substrates for uric acid production. The mean serum uric acid levels were elevated statistically highly significant in type 2 diabetic.⁸ Hyperuricemia is caused by muscle wasting and weight loss in diabetes mellitus¹⁵ Chronic high glucose concentration causes tissue injury, in turn leads to increasing non-protein nitrogen substances. This

phenomenon accounts for increased uric acid levels. Diabetic patients have a high risk of kidney disease due to hyperglycaemia, Hyperuricemia etc. Increased glycaemic index related with Hyperuricemia lead to changes in glomerular permeability. The highly significant values seen were due to dysfunction of the rennin-angiotensin system in long term diabetes. Type 2 diabetic patients have a long asymptomatic period of hyperglycaemia and many other conditions causing micro albuminuria but hypertension and long term diabetes are main risk factors.⁹

We found that out of 112 patients with hypertension, 84 had high and 28 had low serum uric acid level. Out of 56 patients who had not hypertension, 36 had high serum uric acid and 20 had low.

Serum uric acid and urine micro albumin level was elevated with duration of diabetes mellitus. Many studies saw association with poor glycaemic control and creatinine like study by El-Wakf et al.¹⁰ Uric acid levels also serve as an indicator of cardiac risk, which when raised in the cases of type 2 DM, further adds the cardiac risk which is already there due to diabetes.

The prevalence of diabetic peripheral neuropathy shows a significant correlation with increased UA levels.¹⁰ Several studies demonstrated that, when controlled for confounding factors such as age, gender, BMI, renal function, and/or diabetic duration, Serum UA levels were high in patients with diabetic polyneuropathy and sudomotor dysfunction.^{30,32} The pathophysiology of diabetic neuropathy is not completely understood, and multiple metabolic imbalances underlie the development of diabetic neuropathy.⁷⁻¹⁰ Hyperglycemia, dyslipidemia, and cardiovascular dysfunction are all independent risk factors for neuropathy. Probable etiologic factors include the polyol pathway, non-enzymatic glycation, free radicals, oxidative stress, and inflammation. Oxidative stress and inflammation are involved in XDH/XO activity. It is therefore speculated that UA generation by XDH/XO plays a role in diabetic neuropathy.^{5,8,9}

In our study complications are found to have been increased in diabetic patients with Hyperuricemia. The mean serum uric acid and urine micro albumin levels were elevated statistically highly significant in type 2 diabetic. The presence of micro albuminuria is an indicator of the early stages of kidney disease in diabetic

patients. These results were supported by other studies as follows, same finding observed by Cai xiao-ling (2011).¹¹ Chonchol M, (2007)¹² and Saeed Behradmanesh et al (2012).¹³

CONCLUSION

Authors found that elevated serum uric acid levels in type 2 diabetes mellitus cause more micro vascular and macro vascular complications. Further, higher FBS and increasing age are found to be associated with higher uric acid levels.

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