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ORIGINAL RESEARCH

Association of serum uric acid with albuminuria and carotid atherosclerosis in type 2 diabetes mellitus patients

[1]Dr. Rupali J. Kapale, [2]Dr. Amit Porwal, [3]Dr. Rohit Gosavi

[1,2,3]Assistant Professor, Department of General Medicine, Krishna Institute of Medical Sciences, Karad, Maharashtra, India

Correspondence:
Dr. Amit Porwal
Assistant Professor, Department of General Medicine, Krishna Institute of Medical Sciences, Karad, Maharashtra, India

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ABSTRACT

Background: Cardiovascular disease (CVD) is the primary cause of mortality and morbidity in patients with type 2 diabetes mellitus. The present study was conducted to assess association of serum uric acid with albuminuria and carotid atherosclerosis in type 2 diabetes mellitus patients.

Materials & Methods: 65 type II diabetes mellitus patients of both genders were included. In all, uric acid (UA) was measured by enzymatic photometric test, urine albumin was measured by immunoturbidimetric assay, urine creatinine was measured using creatinine Jaffe method and albumin creatinine ratio (ACR) was calculated by dividing urine albumin concentration with urine creatinine concentration.

Results: Out of 65 patients, males were 35 and females were 30. The mean uric acid in males was 6.82 mg/dl and in females was 5.16 mg/dl.Albumin showed normoalbuminuria in 30, micromoalbuminuria in 20 and macromoalbuminuria in 15. IMT was between 0.4-0.5 cm in 12, 0.5- 0.6 cm in 14, 0.6-0.7 cm in 20 and 0.7-0.8 cm in 9 subjects. The difference was significant (P< 0.05). UA had positive correlation with logarithm of urine albumin excretion and IMT (P< 0.05).

Conclusion: Asymptomatic hyperuricemia is highly prevalent in type 2 diabetic patients. Serum UA concentration serves as early and independent marker of renal dysfunction in type 2 diabetic patients. Serum UA concentration serves as early marker of carotid atherosclerosis in type 2 diabetic patients.

Key words: hyperurecemia, micromoalbuminuria, diabetes mellitus

INTRODUCTION

Cardiovascular disease (CVD) is the primary cause of mortality and morbidity in patients with type 2 diabetes mellitus; and several risk factors, including smoking, hypertension, and dyslipidemia, have been shown to accelerate the progression of CVD. Male sex is also an independent risk factor for CVD. Furthermore, elevated urinary albumin excretion has been reported to be associated with increased risk of CVD.[1]

Diabetes mellitus is a heterogeneous group of metabolic disorders causing macrovascular and microvascular (kidney damage) complications.[2] Type 2 diabetes mellitus is characterized by deficiency of insulin, variable degree of insulin resistance, impaired insulin secretion, and impaired glucose utilization. Among individuals with type 2 diabetes mellitus, death from macrovascular disease is more common.[3] Higher levels of serum insulin may decrease uric

acid (UA) clearance by kidneys and predispose to UA injury. Several large epidemiologic studies have reported that elevated serum UA concentration is associated with cardiovascular disease. Microalbuminuria means significant increase in albumin excretion rate (AER) and may reflect a generalized defect in vascular permeability and a concomitant atherogenic diathesis.[4]

Some investigators have suggested that uric acid plays a causal role in the development of CVD whereas others have concluded that uric acid merely reflects other concomitant risk factors, such as hypertension, insulin resistance, or dyslipidemia.[5] The present study was conducted to assess association of serum uric acid with albuminuria and carotid atherosclerosis in type 2 diabetes mellitus patients.

MATERIALS & METHODS

The present study comprised of 65 type II diabetes mellitus patients of both genders. All were informed regarding the study and their written consent was obtained.

Data such as name, age, gender etc. was recorded. In all, uric acid (UA) was measured by enzymatic photometric test, urine albumin was measured by immunoturbidimetric assay, urine creatinine was measured using creatinine Jaffe method and albumin creatinine ratio (ACR) was calculated by dividing urine albumin concentration with urine creatinine concentration. Common carotid artery and internal carotid artery intima-media thickness (in centimetres) of both sides was recorded. The degree of plaque was graded for each segment using the following criteria: Grade 0: no observable plaque, grade 1: one small plaque (< 30% of the vessel diameter), grade 2: one medium plaque (30-50% of the vessel diameter) or multiple small plaques, grade 3: one large plaque (> 50% of the vessel diameter) or multiple plaques with at least one medium plaque. Results were tabulated and assessed statistically. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Total- 65		
Gender	**Male**	**Female**
Number	35	30

Table I shows that out of 65 patients, males were 35 and females were 30.

Table II Assessment of parameters

Parameters	Variables	Mean	P value
Uric acid (mg/dl)	Males	6.82	0.05
	Females	5.16	
Albumin	Normoalbuminuria	30	0.05
	Micromoalbuminuria	20	
	Macromoalbuminuria	15	
IMT	0.4-0.5 cm	12	0.21
	0.5- 0.6 cm	14	
	0.6-0.7 cm	20	
	0.7-0.8 cm	9	

Table II, graph I shows that mean uric acid in males was 6.82 mg/dl and in females was 5.16 mg/dl. Albumin showed normoalbuminuria in 30, micromoalbuminuria in 20 and macromoalbuminuria in 15. IMT was between 0.4-0.5 cm in 12, 0.5- 0.6 cm in 14, 0.6-0.7 cm in 20 and 0.7-0.8 cm in 9 subjects. The difference was significant (P< 0.05).

Graph I Assessment of parameters

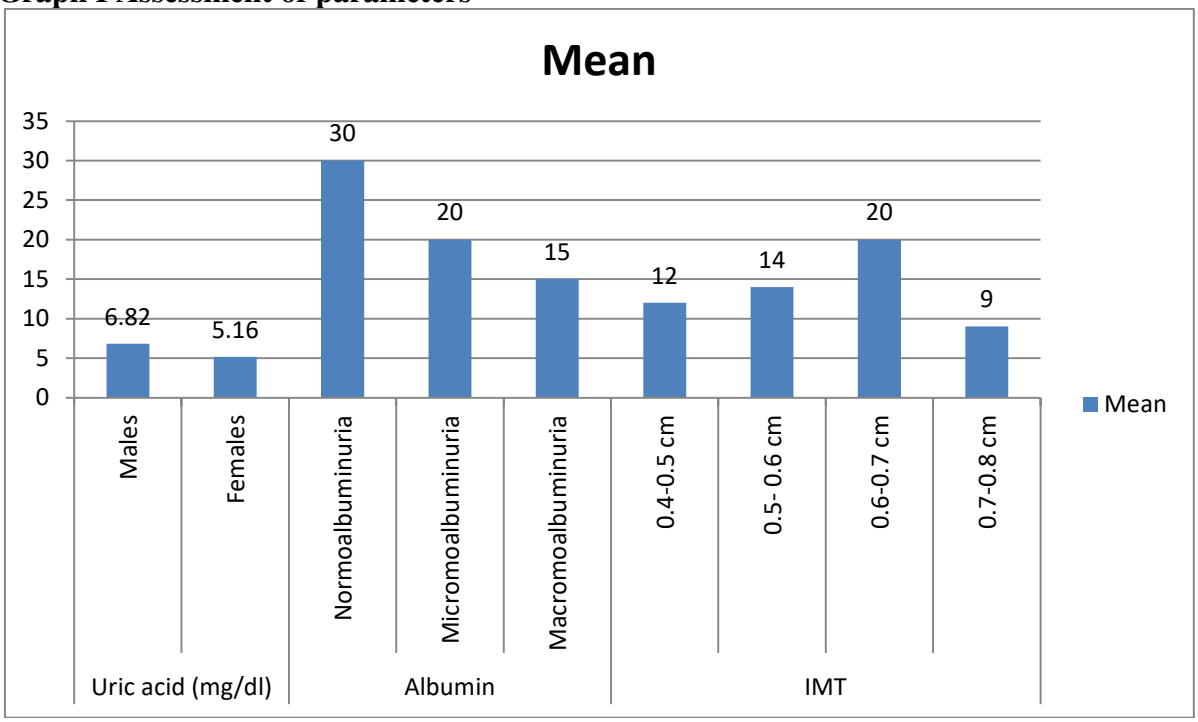

Table III UA correlation with logarithm of urine albumin excretion and IMT

Parameters	Pearson correlation	Significance
Log urine albumin: creatinine	0.325	0.02
IMT	0.382	0.05

Table III shows that UA had positive correlation with logarithm of urine albumin excretion and IMT (P< 0.05).

DISCUSSION

Hyperuricemia has been reported to be associated with increased risk of renal insufficiency as well as cardiovascular events.[6] Epidemiologic studies have found that hyperuricemia is an independent risk factor for renal dysfunction in a general population in patients with hypertension and in patients with diabetes.[7]The present study was conducted to assess association of serum uric acid with albuminuria and carotid atherosclerosis in type 2 diabetes mellitus patients.

We found that out of 65 patients, males were 35 and females were 30. Kang et al[8] hypothesized that elevated serum uric acid levels are a strong predictor of albuminuria in patients with type 1 diabetes. For every 1-mg/dl increase in serum uric acid levels at baseline, there was an 80% increased risk of developing micro- or macroalbuminuria at 6 years. Additional covariates considered in the stepwise model were sex, age, duration of diabetes, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker treatment, waist circumference, waist/hip ratio, body mass index, systolic and diastolic blood pressure, smoking, serum creatinine, cystatin C, high-density lipoprotein cholesterol and triglycerides.

We observed that mean uric acid in males was 6.82 mg/dl and in females was 5.16 mg/dl. Fukui et al[9] evaluated relationships of serum uric acid concentrations to degree of urinary albumin excretion as well as to major cardiovascular risk factors, including age, blood pressure, serum lipid concentration, and glycemic control. The relationships between serum uric acid concentration and pulse wave velocity or ankle-brachial index (n = 236) and between serum uric acid concentration and carotid intima-media thickness or plaque score (n = 125) were investigated additionally in a subgroup of patients. Serum uric acid concentration

correlated positively with logarithm of urinary albumin excretion. Positive correlation was found between serum uric acid concentration and intima-media thickness whereas inverse correlation was found between serum uric acid concentration and ankle-brachial index. Multiple regression analysis demonstrated that serum uric acid concentration (β = .281, P b .0001), duration of diabetes (β = .253, P b .0001), hemoglobin A1c (β = .166, P = .0034), serum triglyceride concentration (β = .125, P = .0472), and systolic blood pressure were independent determinants of logarithm of urinary albumin excretion.

We observed that albumin showed normoalbuminuria in 30, micromoalbuminuria in 20 and macromoalbuminuria in 15. IMT was between 0.4-0.5 cm in 12, 0.5- 0.6 cm in 14, 0.6-0.7 cm in 20 and 0.7-0.8 cm in 9 subjects. We found that UA had positive correlation with logarithm of urine albumin excretion and IMT (P< 0.05). Singh et al[10] found that prevalence of hyperuricemia was found to be high (46%) in type 2 diabetic patients. It was also higher in females (73.7%) than males (25.8%). There was positive correlation between serum UA concentrations with logarithm of urine albumin excretion (P < 0.023) and carotid intima-media thickness (IMT) (P < 0.027). Plaque index also showed a positive correlation with UA (P < 0.019). However, there was no positive correlation with UA and other variable such as age, duration of diabetes, systolic blood pressure, diastolic blood pressure, HbA1c, lipid profiles, urea, and creatinine.

Epidemiologic studies have found that hyperuricemia is an independent risk factor for renal dysfunction in a general population in patients with hypertension and in patients with diabetes.[11] It has been shown that hyperuricemia induced endothelial dysfunction, glomerular hypertension and renal hypertrophy. The main pathophysiologic mechanism by which uric acid causes renal dysfunction involves an inhibition of endothelial nitric oxide bioavailability activation of the rennin angiotensin system and direct actions on endothelial cells and vascular smooth muscle cells.[12]

CONCLUSION

Authors found that asymptomatic hyperuricemia is highly prevalent in type 2 diabetic patients. Serum UA concentration serves as early and independent marker of renal dysfunction in type 2 diabetic patients. Serum UA concentration serves as early marker of carotid atherosclerosis in type 2 diabetic patients.

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