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SERUM URIC ACID LEVEL IN TYPE 2 DIABETES MELLITUS

Medicine

Dr.Priya V. Sutar Assistant Professor, Department of General Medicine, Great Eastern Medical School and Hospital, Srikakulam.

Dr. K Sudheer* Associate Professor, Department of General Medicine, Great Eastern Medical School and Hospital, Srikakulam. *Corresponding Author

ABSTRACT

Background : Cardiovascular disease has emerged as a major health burden worldwide.[1] Type 2 diabetes mellitus is an epidemic in India for the past few decades. Diabetes mellitus is the most important risk factor associated with two to four fold increased incidence of coronary artery disease.[2] But despite abundant epidemiological evidence, the role of increased serum uric acid and cardiovascular risk is controversial. So the aim of this study was to compare the levels of serum uric acid level in Type 2 diabetes mellitus.

Materials and Methods : 70 cases and 30 controls, Among 70 cases studied, there were 43 males and 27 females, among 30 controls there were 18 males and 12 females were included in the study .Serum uric acid was done by using semi auto analyser . Student 't' values was applied for significance. Significance of 'P' value was below 0.05.

Results: The serum uric acid level of diabetics was very much elevated compared with controls and it was highly significant.The prevalence of hyperuricemia is more in diabetic patients when compared to controls. In the study group mean uric acid values were higher in females than males and the difference was statistically significant. Mean value of Serum uric acid level was higher in longer duration (9-12 years) of diabetes 6.87±1.03, when compared to shorter duration (2-4 years) of diabetes 4.31±1.08.

Conclusion : Uric acid level above 4 mg/dl in diabetic population considered as a "Red flag" sign was a marker or risk factor for CAD, which was present in 78% of study population.

KEYWORDS

Introduction

Cardiovascular disease has emerged as a major health burden worldwide.[1] Type 2 diabetes mellitus is an epidemic in India for the past few decades. Diabetes mellitus is the most important risk factor associated with two to four fold increased incidence of coronary artery disease.[2]

Nearly 120 years have elapsed since serum uric acid was first described as risk factor for cardiovascular disease.[3] Serum uric acid as a potential cardiovascular disease risk factor has ballooned in the last several years with numerous abstracts & research papers, multiple editorials & review articles. The four major risk factors for CAD viz, hypercholesterolemia, hypertension, diabetes mellitus, and cigarette smoking which were present in Framingham's cohort are difficult to explain among Indians with CAD. CAD in Indians is present even with low cholesterol level.[4] Obesity, systemic hypertension, hypercholesterolemia is associated with Type 2 DM, as a result of insulin resistance state.[5]

Much but not all epidemiological research identifies hyperuricemia as a independent risk factor for the development of cardiovascular disease, renal disease & stroke, particularly in patients with hypertension or congestive heart failure and in women.[6]

Hyperuricemia has been found to be associated with obesity and insulin resistance, and consequently with type 2 diabetes.[7] Further potentially important biological effects of uric acid relate to endothelial dysfunction by inducing antiproliferative effects on endothelium and impairing nitric oxide production and inflammation.[8,9] Uric acid may play a role in immune activation with subsequent increased chemokine and cytokine expression.[10,11]

Puig et al has found that in patients with metabolic syndrome serum uric acid level was higher when compared with controls and that serum urate increases with the number of components of metabolic syndrome.[12] In addition a recent study in rats showed that fructose – induced hyperuricemia plays a pathogenic role in the metabolic syndrome.[13]

Some have found a significant & specific independent association between uric acid level and cardiovascular mortality and morbidity, while others have come to an opposite conclusion.[14] Thus despite abundant epidemiological evidence, the role of increased serum uric acid and cardiovascular risk is controversial.

Here an attempt has been made to study the level of serum uric acid level in Type 2 diabetes mellitus & the correlation between elevated serum uric acid level and the component of metabolic syndrome like obesity, hypertension, dyslipidemia.

METHODS:

This study was conducted in Great eastern medical school and college, Srikakulam This is a descriptive analytical study conducted between July 2014 to March 2015 on 70 cases. Patients with type 2 diabetes mellitus (patients were taken irrespective of their glycemic control and their duration of diabetes) and who were above 40 years were included of both sexes were included in the study. Patients with renal failure. Pregnancy & lactating mothers, those who were on long term diuretics & steroid, Patients who were regularly consuming alcohol, Patients who were on antimetabolite and chemotherapy drugs, Patients who had hepatic & metabolic disorders, Patients who had PVD/CVA/ Pulmonary Tuberculosis, Renal transplant patients were excluded from the study. Subjects who were above 40 years and had normal blood sugar and who met the above exclusion criteria included as control. The study group thus identified by the above criteria (inclusion and exclusion) were first instructed about the nature of study. Willing participants were taken up after getting a written informed consent from them. Selected socio- demographic, clinical, laboratory data were elicited from the patients and controls and recorded in proforma.

Blood urea estimation was done manually by using diacetyl monoxime method (DAM).Serum creatinine estimation was done by using COBAS auto analyser. Serum uric acid was done by using semi auto analyser. Data was entered in Microsoft excel spread sheet and analysed statistically using standard statistical software. Student 't' values was applied for significance. Significance of 'P' value was below 0.05.

RESULTS:

The total number of subjects included in this study was 100. Among those 100 subjects, 70 were cases (type 2 diabetes mellitus) and 30 were controls (non diabetic).

The age of the subjects in the study group ranged from 43 to 72 years. The mean and standard deviation for age of the cases and controls were 59.13±9.11 and 56.97±8.41 respectively, there was no significant difference among the cases and controls with reference to the age. The distribution of cases and controls in relation to age is provided in table 2 given below.

Among 70 cases studied, there were 43 males and 27 females, among 30 controls there were 18 males and 12 females. The details are given in table 3 provided below. The sex composition of the study group and control group does not differ.

Among 70 cases and 30 controls screened for BMI, none were obese. The mean and standard deviation for BMI of cases and controls were 24.93 ± 3.13 and 21.8 ± 2.3 respectively. The mean and standard deviation for fasting blood sugar was 132.79±36.72 similarly for post prandial blood sugar was 206.02 ± 37.49 among diabetes. Thus showing their diabetic status was under the control.

There was no significant difference between cases and controls in relation to selected cardiovascular risk factors. Serum uric acid in the study population and control varied from 2.8 to 8.3 and 2.9 to 5.3 mg/dl respectively. The mean and standard deviation of uric acid among cases was 5.25 ± 1.59 while in control it was 3.91 ± 0.98 respectively.

Results:

Table 1 : Serum Uric Acid level in diabetics and controls

	Cases		Controls	
Serum Uric Acid*	Mean	S.D.	Mean	S.D.
	5.25	1.59	3.91	0.98
* P value : 0.0001 (significant)				

The serum uric acid level of diabetics was very much elevated compared with controls and it was highly significant.

Table 2 : Hyperuricemia in Cases and Controls

Hyperuricemia	Cases				Controls			
	No	%	Mean	S.D	No	%	Mean	S.D
+	15	21.4	7.16	0.5	0	-	-	-
-	55	78.67	4.73	1.21	30	100%	3.91	0.98

*P = 0.0001 (Significant)

This table clearly shows that the prevalence of hyperuricemia is more in diabetic patients when compared to controls. In the study group mean uric acid values were higher in females than males and the difference was statistically significant.

The mean value of serum uric acid was 6.13 ± 1.45 in those with BMI > 25. It was significantly higher than compared to those having BMI < 25. The mean value of serum uric acid in BMI < 25 was 4.13±1.23.

Uric acid level increases with increased WHR. The WHR abnormality was considered in 33 cases based on, WHR above 1.0 for men, above 0.8 for women and correlated with uric acid level was significant.

Mean value of Serum uric acid level was higher in longer duration (9-12 years) of diabetes 6.87±1.03, when compared to shorter duration (2-4 years) of diabetes 4.31±1.08. This is shown in table 16 given below:

Table 3 : Duration of Diabetes and Hyperuricemia

DOD	No.	Mean	S.D.
2-4 years	12	4.31	1.08
5-8 years	37	5.01	1.891
9-12 years*	21	6.87	1.03

* P Value = 0.001 (Significant)

Uric acid level increases with increasing duration of diabetes and it was statistically significant.

Discussion :

Diabetes is the most common risk factor for cardiovascular disease, and it is present in nearly 25% adults and increases in prevalence with age.[15] "In the absence of gout the presence of hyperuricemia in patients with type 2 diabetes mellitus is an important marker as well as an added risk factor for atherosclerosis." [16] In this study the relation between serum uric acid level and diabetes was examined. Uric acid is a marker for CAD in combination with other risk factors among diabetics. Though uric acid level and age was independent it is possible that duration of the illness may have an impact on uric acid levels.

In the present study females have higher uric acid level when compared to males. The mean uric acid value in males was 5.06±1.64while in females it was 5.93±1.13, and the difference was statistically significant in this study. The possible reasons for such difference may be attributable to increased BMI and increased WHR among women.

In the present study serum uric acid correlated well with body mass index (BMI). The mean uric acid in those subjects with BMI > 25 was higher than those with BMI < 25 (6.13±1.45 Vs 4.13±1.23) and the difference was statistically significant. Rathmann et al., assessed the various components of insulin resistance syndrome in young black and white adults. They concluded that body mass index showed strongest positive correlation with the uric acid among insulin resistant components.[17,18]

Waist hip ratio is an important measure of obesity, especially central obesity. Intraabdominal fat has significant implication for morbidity than subcutaneous fat present in buttocks and extremities.[19]

Abdominal obesity is a component of metabolic syndrome. Waist circumference > 102 cm in men and >88cm in women isabnormal. In this study patient with higher waist hip ratio had higher uric acid level when compared with low waist hip ratio.

The mean uric acid value in patients with waist hip ratio abnormality and patients without waist hip ratio was 5.93±1.38 and 4.63±1.3 respectively and the difference was statistically significant. Patients with Poor metabolic control and longer duration of diabetes were more susceptible to develop various complications including hyperuricemia.[19] Our study also shows that higher level of serum uric acid was seen in patients with longer duration of diabetes when compared with shorter duration of diabetes, 6.87±1.03 (9-12yrs) vs 4.31±1.08 (2-4yrs) This difference was statistically significant.

Uric acid >4 mg/dl should be considered as a "Red flag" in those patients at risk for cardiovascular disease.[20] In this study 78.57% of diabetic patients have serum uric acid level >4 mg/dl, while only 30% of the control have serum uric acid >4mg/dl. In these patients the clinician should strive to utilize global risk reduction programme to reduce the complications of atherogenic process.

The association of serum uric acid with cardiovascular disease has been appr eciated for nearly half a century. However, its role as a cardiovascular risk factor remains controversial.[21] In an epidemiologic follow up study an association between serum uric acid and cardiovascular disease was shown. The PIUMA study [22] also concluded that raised serum uric acid is a powerful risk marker for subsequent cardiovascular disease and all cause mortality. Of the 70 cases of type 2 diabetes mellitus, hyperuricemia was observed in 15 patients which accounts for 21.43% of cases. Canon[23] showed a prevalence of hyperuricemia in 25% of longstanding uncontrolled diabetes. But in this study many of the cases were on treatment which might have affected the results. A large body of evidence links uric acid with metabolic syndrome of insulin resistance, obesity, hypertension and dyslipidemia. In this study relationship between obesity, hypertension, dyslipidemia and hyperuricemia was statistically significant.

Because of limited resources GTT, HbA_1C, leptin level, C peptide assay, plasma insulin assay could not be tested. X ray chest was not performed is every case due to technical limitation. Only serum uric acid levels were analysed. Urinary excretion and urate clearance was not done.

Uric acid was significantly elevated in diabetic population. The serum uric acid level was independent of age and smoking status in males. Significant correlation was noticed between serum uric acid and BMI as well as WHR. Significant elevation of uric acid level was observed more among females. Elevated uric acid levels were significantly noticed among those with hypertension, dyslipidemia, coronary artery disease and chronicity of the diabetes.

Uric acid level above 4 mg/dl in diabetic population (considered as a "Red flag" sign) was a marker or risk factor for CAD, which was present in 78% of study population.

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