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Biochemistry

KEY WORDS: Diabetes mellitus, Fasting blood sugar, Serum uric acid, Serum creatinine.

A STUDY OF SERUM URIC ACID LEVELS IN TYPE 2 DIABETES MELLITUS CASES AND ITS COMPARISON WITH THE SERUM CREATININE LEVELS

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ABSTRACT

BACKGROUND: Type 2 Diabetes Mellitus is a major non-communicable disease resulting from insulin resistance and is associated with cardiovascular, neurological and renal complications. Recent studies show association of hyperuricemia and Diabetes Mellitus. Uric acid increases oxidative stress that leads to vascular dysfunction and high intra glomerular pressure leading to renal complications. High serum creatinine is an indicator of renal compromise.

OBJECTIVES: To evaluate serum uric acid and serum creatinine levels in type 2 diabetes mellitus patients and to find association between them.

METHODOLOGY: The study was conducted in Osmania general hospital. Fifty cases of established Type 2 Diabetes Mellitus formed the study group and 50 normal healthy individuals formed the control group. Serum uric acid, Fasting Blood Glucose (FBS) and serum creatinine were estimated by colorimetric enzymatic methods on Beckman coulter AU5800. Mean values were compared in cases and controls using student t- test. Study group was further studied under 2 subgroups with serum Uric acid < 7 mg/dl and ≥7 mg/dl. In these 2 subgroups the association of Serum uric acid with FBS and creatinine was analysed statistically.

RESULTS: Serum uric acid were found high in cases(7.63+/- 3.36)as compared to controls(4.48+/- 1.09) p value < 0.001.Serum creatinine were also high in cases(1.59+/- 1.39)as compared to controls (0.87+/- 0.29) p value <0.005.Study subgroup with serum uric acid ≥7 mg/dl was associated with high creatinine and high fasting blood sugar levels when compared to subgroup with serum uric acid <7 mg/dl.

CONCLUSION: Our study showed increased serum uric acid and serum creatinine levels in cases when compared to controls. There was significant association between high serum uric acid and high creatinine levels in cases. Therefore, it is important to measure serum uric acid and serum creatinine levels in diabetics for early detection of renal pathology.

BACKGROUND

INTRODUCTION:

According to WHO, Diabetes Mellitus is defined as a metabolic disorder of multiple aetiology, characterised by chronic hyperglycaemia along with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion or insulin action or both(1). Diabetes mellitus is one of the major non-communicable diseases and is a leading public health problem with increasing incidence and long term complications such as diabetic nephropathy, diabetic neuropathy, diabetic retinopathy etc., which are mainly a consequence of macro and micro vascular damages of the target organs. The international federation of diabetes reported that adults suffering from diabetes all over the world are around 415 million and this estimation is likely to reach around 642 million by 2040(2). The worst affected age group is between 40-59 years (3). Risk factors contributing to diabetes mellitus include obesity, unsatisfactory diet, sedentary lifestyle and increasing urbanisation. The cause of clinical diabetes includes both absolute and relative deficiencies of insulin. Type 1 diabetes mellitus is due to insulin deficiency caused by autoimmune destruction of beta cells in the islets of pancreas (4). Type 2 diabetes mellitus is characterised by insulin resistance and impaired insulin receptors.

Uric acid is the end product of purine metabolism in humans. Uric acid production varies with the purine content of the diet, rate of purine biosynthesis, degradation and salvage pathway (5, 6). Hyperuricemia is defined by serum uric acid concentration greater than 7.0 mg/dl in men or greater than 6 mg/dl in women. Many studies revealed that hyperuricemia is associated with CVD and premature deaths from MI and stroke (7, 8). Recent studies have demonstrated that serum uric acid levels are higher in subjects with pre-diabetes and early type 2 diabetes than in healthy controls(9). Current hypothesis states that oxidative stress is a common pathogenic factor leading to diabetes. Free radicals are generated during uric acid production, thus uric acid levels might indicate excessive oxidative stress. Hyperuricemia has also been added to the set of metabolic abnormalities associated with insulin resistance in metabolic syndrome (10, 11, and 12).

Serum Creatinine is known to be raised with hyperglycaemia in diabetes, usually correlating with kidney damage severity. This study was designed to evaluate the levels of serum uric acid in type 2 diabetes mellitus patients and to compare with serum creatinine levels.

MATERIALS AND METHODS:

This is a case control study conducted in Osmania General Hospital in the month of September 2020. Both male and female subjects were included in the age group of 35-70 years. Prior consent was taken.

INCLUSION CRITERIA: (I) 50 patients who were diagnosed clinically and biochemically as Diabetes Mellitus based on ADA guidelines attending out-patient department were enrolled for the study. (ii) 50 normal healthy individuals were included as controls in the study.

EXCLUSION CRITERIA: (a) pregnancy (b) patients with renal stones and renal failure (c) liver diseases (d) drugs affecting renal function and uric acid levels (e) any other systemic illness that may affect the renal function.

- Study subjects had undergone clinical examination.
- 3ml of fasting venous blood was collected into grey vacutainer in both cases and controls and fasting blood sugar levels were measured by enzymatic method on Beckman coulter AU5800.
- 5ml of venous blood was collected into red vacutainer, serum was separated and serum uric acid and serum creatinine levels were measured by enzymatic methods on Beckman coulter Au5800.

STATISTICAL ANALYSIS:

- From our data, the mean, percentage, standard deviation, chi-square test and multiple correlations were done by using SPSS-10.
- The p value was used to compare the cases mean value with control mean value and the p value of <0.005 was considered statistically significant.

RESULTS:

The study included 50 cases and 50 healthy controls. The study group was further studied under 2 sub-groups with serum uric acid <7mg/dl and >/=7mg/dl.In these 2 sub-groups the association of Serum uric acid with Fasting blood sugar levels between 125-200mg/dl and >200mg/dl and serum creatinine levels <1.3mg/dl and >/= 1.3mg/dl were analyzed statistically.There were 46 females and 54 males in our study.The mean for age in the cases and controls were 56.04+/- 13.46 and 53.83+/-10.64 respectively (table no.1).

Table no.1: Age distribution

	Cases	Controls
No. of study subjects	50	50
Age (years) mean +/-SD	56.04+/-13.46	53.82+/-10.64

The Fasting Blood Sugar(FBS) of the cases and controls had mean of 189.9 +/- 46.30 and 97.4 +/- 15.50 respectively.Majority of the cases (56%) had FBS levels between 125-200mg/dl while 44% of the cases had FBS levels of >200mg/dl.Mean serum uric acid levels in cases and controls were 7.63 +/- 3.36 and 4.48 +/- 1.09 respectively.Mean serum creatinine levels in cases & controls were 1.59 +/- 1.39 and 0.87 +/- 0.29 respectively.P value for all the parameters were considered statistically significant (table no.2).

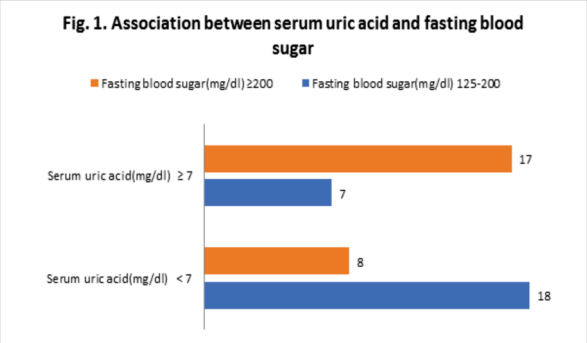
Table no. 2: Comparison of study parameters in cases and controls

parameters	Cases mean +/- SD	Controls mean +/- SD	P value
Fasting blood sugar(mg/dl)	189.9 +/- 46.30	97.4 +/-15.50	< 0.001
Serum uric acid(mg/dl)	7.63 +/- 3.36	4.48 +/- 1.09	< 0.001
Serum creatinine(mg/dl)	1.59 +/- 1.39	0.87 +/- 0.29	< 0.005

Out of 25 of the study subjects with FBS levels between 125-200mg/dl, 18 had serum uric acid levels of < 7mg/dl and 7 had uric acid levels of ≥7mg/dl.Out of 25 of the study subjects with FBS levels of >200mg/dl, 8 had serum uric acid levels of <7mg/dl and 17 had ≥7mg/dl.There was significant association seen between FBS levels and serum uric acid levels in the study subjects(p<0.001) (table no.3,fig.1).

Table no. 3: Association between serum uric acid and fasting blood sugar (Fig. 1.)

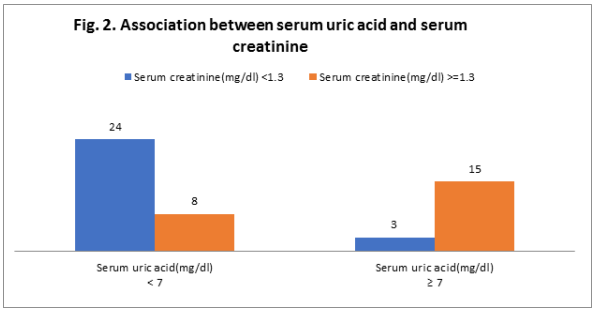
Serum uric acid(mg/dl)	Fasting blood sugar(mg/dl)		Total
	125-200	≥200	
< 7	18	8	26
≥ 7	7	17	24
Total	25	25	50



Out of 27 of the study subjects with serum creatinine levels of <1.3mg/dl, 24 had serum uric acid levels of <7mg/dl and 3 had ≥7mg/dl.Out of 23 of the study subjects with serum creatinine levels of ≥1.3mg/dl, 8 had serum uric acid levels of <7mg/dl and 15 had ≥7mg/dl.There was significant association seen between the serum uric acid and serum creatinine levels in the cases (p<0.001). We observed that with elevated serum creatinine levels, there was also increase in serum uric acid levels (table no.4, fig.2).

Table no. 4: Association between serum uric acid and serum creatinine (Fig. 2.)

Serum uric acid(mg/dl)	Serum creatinine(mg/dl)		Total
	< 1.3	≥ 1.3	
< 7	24	8	32
≥ 7	3	15	18
Total	27	23	50



DISCUSSION:

Diabetes mellitus is a chronic disorder that is associated with cardiovascular, renal and various types of microangiopathies including metabolic syndrome. Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance or hyperinsulinemia in metabolic syndrome. Oxidative stress is a common pathogenic factor leading to diabetes. Free radicals are generated during uric acid production, thus uric acid levels might indicate excessive oxidative stress.

In our study we measured serum uric acid levels in diabetes mellitus patients and compared it with the normal healthy individuals. The mean uric acid level was significantly high in the study group (7.63 +/- 3.36) when compared to the control group (4.48 +/- 1.09) and the p value is found statistically significant.

The mean serum creatinine level was also high in the study group (1.59 +/- 1.39) when compared to the control group (0.87 +/- 0.29) and the p value is found statistically significant. There was significant association seen between serum uric acid and serum creatinine levels in cases (p < 0.001).

Uric acid is the ultimate product of purine metabolism in the human body (13). Serum uric acid has been suggested to be associated with risk of type 2 diabetes mellitus. Fructose is the main component of added sugar which causes mitochondrial oxidative stress (14, 15) and inhibits AMPK (16) and the subsequent intracellular ATP depletion (17) and nucleotide turnover leads to a significant increase in serum uric acid (18). Excessive uric acid leads to an increase in reactive oxygen species (ROS) production, which results in inflammation and dysfunction in the vessels (19). This oxidative stress can affect the expression of insulin gene causing decrease in insulin secretion (20).

Creatinine is the breakdown product of creatinine phosphate is released from skeletal muscle at a steady rate. It is filtered by the glomerulus, and a small amount is also secreted into the glomerular filtrate by the proximal tubule (21) and therefore it is helpful for tracking the progression of diabetic kidney disease.

Bombelli et al (22, 23) conducted a study among 3200 northern Italian residents between the ages of 25 and 74 and found that increased uric acid resulted in an increased risk of impaired fasting glucose (IFG), and people with higher median uric acid levels may also develop metabolic syndrome and diabetes. Similar studies were conducted by Yan et al (24), Kuwata (25), Du et al. (26) and found hyperuricemia associated with diabetes and its complications.

Biologically, uric acid plays an important role in worsening of insulin resistance by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake. 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. Therefore it remains controversial whether serum uric acid is independently associated with the development of type 2 diabetes mellitus.

As many studies supports the present study, analysis of serum uric acid and serum creatinine in type 2 diabetic subjects may be used as an associated biochemical parameter to follow the course of the disease and to assess any complications are going on as seen in advanced diabetic cases.

CONCLUSION:

Our study showed increased serum uric acid and serum creatinine levels in cases when compared to controls. It is also seen that there was significant association between serum uric acid and creatinine levels in cases. Therefore it is important to evaluate serum uric acid and serum creatinine levels routinely in diabetes mellitus patients for screening of further complications.

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