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To Study Serum Uric Acid In Type 2 Diabetes Mellitus Patient

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Abstract
Aims: *To Study Serum Uric Acid Level in Patients With Type 2 Diabetes Mellitus and also association of uric acid level in Patients having Diabetes Mellitus With Coronary Artery Disease.*
Materials and methods*: The study was conducted J.A.Group of Hospital during the period of June 2013 to November 2014 and included about 100 patients of type 2 diabetes mellitus. In addition 50 patients were randomly selected ,who were admitted or attending the OPD of JAH Group of hospital, Gwalior, M.P. were enrolled in the present study as Controls who were Non Diabetic. Total diabetic patient were divided in known cases of diabetes and new casesof diabetes*
Results: *Mean serum uric acid of all cases of DM Type 2 (5.54 ± 1.25 mg/dl) was significantly higher than controls (3.35 ± 0.58 mg/dl). In patients with Known Case of DM Type 2 mean serum uric acid was 6.14 ± 0.95 mg/dl and was significantly higher than new case of DM Type 2 (4.23 ± 0.70 mg/dl) and controls. In Patients with Known Case of Diabetes Mellitus, Mean serum Uric Acid in patients with CAD (6.70 ± 0.69 mg/dl) was significantly higher than Non CAD (5.21 ± 0.46 mg/dl). In Overall diabetes with CAD patients, Serum Uric acid >7.0 was in 14 out of 49 patients while in patients without CAD Uric acid ≤7.0 in all 51 and was significant.*
Conclusion: *It was concluded that the complication of diabetes such as coronary artery disease was prevalent more in known cases of diabetes mellitus and Prevalence was less in the newly diagnosed DM type 2 patients. Mean Serum Uric acid level was in the higher in all diabetic patients (both known & newly diagnosed) with respect to control. Mean Serum Uric acid level was higher in patients with history of diabetes as compared to newly diagnosed as well as controls. In cases of diabetes mellitus serum uric acid level >7.0 mg/dl was significantly seen in cases with diabetes with CAD. Serum Uric acid ≤ 4.0 mg/dl was significantly seen in case without CAD. This data shows hyperuricemia is a significant risk factor for CAD in DM Type2 and hyperuricemia is significantly associated with progression of DM.*
Key words*: Coronary Artery Disease ,Type 2 Diabetes Mellitus, Uric Acid*

I. Introduction

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate. Over the past 30years, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people. [1] It has been estimated that the global burden of type 2 diabetes mellitus for 2010 would be 285 million people (2010) which is projected to increase to 438 million in 2030. [2] Diabetes mellitus is a chronic disease characterized by relative or deficiency of insulin, resulting in glucose intolerance. [2] Hyperuricemia is a condition that is significantly associated with markers of metabolic syndrome such as dyslipidemia, glucose intolerance, high blood pressure, and central obesity, which are accepted as risk factors for developing cardiovascular disease. Hyperuricemia is probably associated with glucose intolerance due to various mechanisms, however, the most important is the association between insulin and renal resistance to absorption of urates. [1,2,3] Diabetic patients with type 2 diabetes mellitus are at greater risk of developing vascular diseases because of lipid changes. It has been well observed that controlling diabetes and lipid levels provide great benefit to diabetic patients. Impaired function of endothelium is an early indicator of cardiovascular discase. A normal endothelium is defined as blood flow response to a vasodilator which is denoted as increased vascular risk. Lipid abnormalities in type 2 diabetic patients with increased serum triglycerides, very low density lipoproteins, low density lipoproteins and lowering of high density lipoproteins. Inslulin resistance syndrome has been widely found that it is associated with type 2 diabetes mellitus in which high density lipoprotein is quite reduced and chances of cardiovascular complication.

II. Materials And Methods

The present study was conducted in J A group of hospital, Gwalior, M.P. (G.R. Medical College, Gwalior, M.P.)

Study Design The present study is a cross sectional study, conducted over a period between May 2013 to November 2014 on the patients of type 2 diabetes mellitus. All the patients of type 2 diabetes mellitus, who are admitted in JAH Group of hospital, Gwalior, M.P. were enrolled in the present study.Total of 100 patients were

included in the study. In addition 50 patients were randomly selected ,who were admitted or attending the OPD of JAH Group of hospital, Gwalior, M.P. were enrolled in the present study as Controls who were Non Diabetic, diagnosed by screening FBS, RBS and without any symptoms of hyperglycemia.

Inclusion criteria :

Cases were classified into Known Cases of Diabetes and New Cases of Diabetes

1. **Known Case Of Diabetes**
- Patient with type 2 diabetes mellitus and already on treatment.

2. **New Case Of Diabetes**
- Patient with fasting blood sugar >126mg/dl and/or post prandial blood glucose >200mg/dl.
- RBS>200mg/dl symptoms of diabetes (polydypsia, polyuria and polyphagia).

3. **Non diabetics (controls)**

Exclusion criteria :
- Patient with creatinine >1.4mg/dl.
- Patient with stress hyperglycemia.
- Patient with uricosuric drugs.
- Patient with malignancy.
- Patient taking long time salicylates

All the patients studied underwent-Detailed history was taken for diabetic symptoms .diabetes onset, treatment and diabetic complication. Detailed history with special emphasis on a systemic quantification of risk factors for atherosclerosis and on atherosclerotic events.Smoking was assessed by history**.**Alcoholic was assessed by history**.**Family history for diabetes and heart disease was emphasized**..**Thorough general physical examination including anthropometric measurement in the form of height, weight, BMI and systemic examination was done.Biochemical investigation with standard laboratory technique in the form of CBC, fasting and post-prandial blood glucose estimation, urine examination, glycosylated hemoglobin estimation (HPLC method), lipid profile, blood urea, uric acid and serum creatinine estimation were done.Serum uric acid was measured with reagent of Trinder's reaction, enzymatic and Calorimetry method, on the principal of uricase-peroxidase method. Intensity of color formed in the reaction is proportion to uric acid concentration.Serum uric acid measurement was repeated if abnormally high levels were present.If uric acid was measured multiple times mean uric acid level was considered**.**Diabetic nephropathy was assessed by serum creatinine and Urine Routine microscopy and 24 hour urine protein for albuminuria.Each patient's serum creatinine, USG (abdomen) and urine albumin was done to assess his kidneys functional status**.**CAD was assessed by history, clinical features such as chest pain, breathlessness, ghabrahat, ECG and cardiac biomarkers and past medical records. Patients were considered as type 2 diabetic as per American Diabetes Association (ADA) 2011, criteria 30 (based on consensus expert from National Data Diabetic Group and WHO).Dyslipidemia was defined using the National Cholesterol Education Programme (NCEP) ATP III guidelines.

Statistical Methods-Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) and chi square test has been used to analyze the data having ordinal variables.Significant figures were analyzed, Suggestive significance (P value: 0.05<P)

Statistical software The Statistical software namely EPI Info 7.0 and Vassar stats (www.vassarstats.net) for the analysis of the data and Microsoft word and Excel were used to generate graphs, tables. A p value of <0.05 was considered as significant.

III. Results

Table No. 1-Distribution of Study Population according to Sex

SEX	Known Case Of type 2 Diabetes Mellitus		New Case Of type 2 Diabetes Mellitus		Significance
	No	Percent	No	Percent	
Female	31	44.93%	8	25.81%	P=0.07 Not Significant
Male	38	55.07%	23	74.19%	
Total	69	100.00%	31	100.00%	

In 69 cases of Known Cases of Type 2 DM Majority were male with 55.07%.
While in 31 cases of New Cases of Type 2 DM 75% were male. Male: female 2.9:1.

Table No. 2-Comparison of serum uric acid level in patients with Known cases, New cases and Total cases with each other and Controls

Comparative Groups		Total No.	Mean	S.D.	Significance
K/C/O DM Type 2 Vs Controls	K/C/O DM Type 2	69	6.14	0.95	P=0.0001
	Controls	50	3.35	0.58	
N/C/O DM Type 2 Vs Controls	N/C/O DM Type 2	31	4.23	0.70	P=0.14
	Controls	50	3.35	0.58	
K/C/O DM Type2 Vs N/C/O DM Type 2	K/C/O DM Type 2	69	6.14	0.95	P=0.02
	N/C/O DM Type 2	31	4.23	0.70	
All Cases Of DM Type 2 Vs Controls	Cases Of DM Type 2	101	5.54	1.25	P<0.0001
	Controls	50	3.35	0.58	

- In patients with K/C/O DM Type 2 have mean serum uric acid of 6.14 ± 0.95 mg/dl and was more than N/C/O DM Type 2 and controls and was ***Statistically Significant with P= 0.0001 and P=0.002 respectively.*** Mean serum uric acid of All cases of DM Type 2 was higher than controls with value 5.14 ± 1.25 mg/dl and was statistically ***Significant with P < 0.0001.***

Table No. 3-Distribution of Study Population according to CAD between known and new cases of diabetes

CAD	Known Case Of type 2 Diabetes Mellitus		New Case Of type 2 Diabetes Mellitus		Significance
	No	Percent	No	Percent	
Absent	26	37.68%	25	80.65%	P = <.0001 Significant
Present	43	62.32%	6	19.35%	
Total	**69**	**100.00%**	**31**	**100.00%**	

- In 69 cases of Known Cases of Type 2 DM, Majority 43 (62.32%) was having CAD.
- While in 31 cases of New Cases of Type 2 DM, Majority 26 (80.65%) were not having CAD.
- CAD in Known Cases of Diabetes was significantly higher than New Cases of DM Type 2 and Controls.

Table No. 4-Distribution of Control Population According To CAD And Their Comparison With All Cases

Sub-Group		Case Of type 2 Diabetes Mellitus		Controls		Significance
		No.	%	No.	%	
CAD	Present	49	49.00%	12	24.00%	P=0.003
	Absent	51	51.00%	38	76.00%	

- In 50 controls, majority was having Non CAD patients are predominant. In comparison to cases these were having significant statistical difference.

Table No.5- Comparison Of Mean Of Serum Uric Acid According To CAD In Diabetes Mellitus

Sub-Groups		Total No.	Mean	S.D.	Significance
CAD in k/c/o DM	Present	43	6.70	0.69	P=0.02
	Absent	26	5.21	0.46	
CAD in n/c/o DM	Present	06	5.33	0.36	P=0.57
	Absent	25	3.97	0.45	

- Mean Serum Uric Acid in patients with CAD was more than rest with 6.70 ± 0.69 mg/dl and it was ***Significant*** with **P= 0.02**.

Table No.6-Comparison Of Level Of Serum Uric Acid In all cases of Diabetes Mellitus on the basis of CAD

Serum Uric Acid	CAD Present	CAD Absent	Significance
≤4.0	00	11	P<0.0001
4.1-7.0	35	40	P= 0.42
>7.0	14	00	P<0.0001

In cases of diabetes mellitus on the basis of CAD, Serum uric acid level >7.0 was seen only in cases with CAD present and data was highly significant. Serum Uric acid ≤ 4.0 in cases without CAD this data was also significant. This data shows hyperuricemia was significant risk factor for CAD.

Table No.7-Comparison Of Serum Uric Acid Level In Patients of Both Known & New Case Of Diabetes Mellitus on The Basis of CAD

Serum Uric Acid	CAD Present	CAD Absent	Significance
≤7.0	35	51	P<0.001 Significant
>7.0	14	0	

- In Overall diabetes with CAD Serum Uric acid is >7.0 in 14 out of 49 patients while in patients without CAD Serum Uric acid ≤7.0 in all 51 and it is ***Significant by Chi-Square test with P<0.001.***

IV. Discussion

In this study mean serum uric acid level in patients with type 2 Diabetes mellitus was 5.54 ± 1.25mg/dl. In patients who were previously diagnosed with Diabetes mellitus and were on treatment had mean serum uric acid level of 6.14 ± 0.95mg/dl, while patients with newly diagnosed Diabetes mellitus had mean serum uric acid level 4.23 ± 0.70. Controls had a mean serum uric acid level 3.35 ± 0.58.

Serum Uric Acid in Patients with Known Case of Type 2 DM Vs New Case Of Type 2 DM Vs Controls

In patients with Known Case Of DM Type 2 mean serum uric acid was 6.14 ± 0.95 mg/dl and was significantly more than New Case Of DM Type 2 and controls. Mean serum uric acid of all cases of DM Type 2 was significantly higher than controls with value 5.54 ± 1.25 mg/dl .In **Sudhindra Rao M. study**[4] mean serum uric acid level was lower in control group (3.84mg/dl), rose in pre-diabetics (4.88mg/dl) and again decreased in diabetics (3.78mg/dl).**M. Modan**[5] study concluded that elevated serum uric acid is a feature of hyperinsulinaemia/insulin resistance. **Nakanishi N et al**[6] study, found that Serum Uric Acid level is closely associated with an increased risk for hypertension and IFG or Type II diabetes.

Mean Uric Acid according to CAD in diabetics and controls :-

Study First Author	Total No of Cases	Serum Uric Acid (mg/dl)
Medalie[7]	344	4.8
Ohlson[8]	47	5.3
Perry[9]	194	6.0
Meisinger[10]	128 men 85 women	5.8
Lin[11]	27 Men 21 Women	5.7 4.0
Chien[12]	548	5.6
Dehghan[13]	462	5.4
Nan[14]	337 Men 379 Women	6.6 5.0
Kramer[15]	55	5.7

In Known Case Of DM Type 2 group, patients with history of CAD had higher mean serum uric acid with value 6.70 ± 0.69 mg/dl and was significantly higher than Non CAD group.In New Case Of DM Type 2 group; Mean serum uric acid was higher in CAD with values 5.33 ± 0.36 mg/dl. **Nadkar MY and Jain VI**[16] found serum uric acid levels were higher in patients of acute myocardial infarction(CAD) correlated with Killip class. There was no significant difference in serum uric acid levels as regards sex, hypertension and diabetes mellitus in patients with MI; however those with history of MI in the past had higher serum uric acid levels. Serum Uric acid of patients was 5.23±1.95 and controls were 3.78±0.74. Hypertensives had serum Uric acid

5.38±2.05, Diabetes mellitus patients had serum Uric acid 5.50±2.14 . In Previous IHD cases serum Uric acid 7.07 ±2.024 . This value is consistent with our study. In study by **Uzma Bano[17] et al** on 66 Congestive Heart Failure patients among the 24 diabetics, 14 (58.3%) had hyperuricemia with mean 9.31 ± 1.72. As consistent with our study hyperuricemia was significantly associated only with CAD. In 1999, the **Chu NF et al[18]** study, in middle aged Taiwan male showed that, hyperuricemia is significant higher in CAD patients.

Serum Uric Acid in Patients with Type 2 DM with CAD In Patients with DM Type 2 serum Uric acid >7.0 was significantly associated with Uric acid was significantly higher in CAD patients with Known Case Of DM Type 2 in earlier observations by student T test Thus Hyperuricemia is predictor or a risk factor for CAD .

V. Conclusion

: It was concluded that the complication of diabetes such as coronary artery disease was prevalent more in known cases of diabetes mellitus and Prevalence was less in the newly diagnosed DM type 2 patients. Mean Serum Uric acid level was in the higher in all diabetic patients(both known & newly diagnosed) with respect to control. Mean Serum Uric acid level was higher in patients with history of diabetes as compared to newly diagnosed as well as controls. In cases of diabetes mellitus serum uric acid level >7.0 mg/dl was significantly seen in cases with diabetes with CAD. Serum Uric acid ≤ 4.0 mg/dl was significantly seen in case without CAD. This data shows hyperuricemia is a significant risk factor for CAD in DM Type2. Hyperuricemia is significantly associated with progression of DM and can increase the morbidity and mortality from diabetes if not manage in time.

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