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# Study of Serum Uric Acid Levels in Type 2 Diabetes Mellitis Patients

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***Abstract***
***Background:*** *Diabetes Mellitus is a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Serum uric acid has emerged as a potential risk factor for type 2 diabetes mellitus. Elevated uric acid levels are often found in individuals with the metabolic syndrome, a collection of risk factors for T2DM often found together, including the following: truncal obesity, hypertriglyeridemia, decreased high density lipoprotein, hypertension, and insulin resistance.*
***Aims And Objectives:*** *Estimation of uric acid levels in Type 2DM.To find correlation between uric acid and glycaemic status in Type 2DM.*
***Material And Methods:*** *Patients diagnosed of type 2 diabetes mellitus in the age group 30-70 years visitng OPD and Indoor of MMIMSR, Mullana, Ambala,India during Oct 2013 to Dec 2015. Type1 diabetes mellitus patiens,diagnosed systemic arterial hypertension, individuals known to have cardiovascular disease, individuals who had cerebrovascular disease, patient with pre existing renal disease, individuals diagnosed as suffering from gout were excluded.*
***Results****: In our study strength of association between the FBS, RBS, HbA1c and Uric acid is high and they are negatively correlated. Mean value of uric acid was highest (4.472mg/dl) if the HbA1c values were less than 7% and it decreased thereafter.*
***Conclusion:*** *Serum Uric acid levels are inversely associated to diabetes mellitus type 2 in both men and women. Uric acid is inversely related to FBS, RBS and HbA1c.*
***Keywords:*** *FBS, RBS, Serum Uric acid levels, HbA1c, Diabetic patients*

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## I. Introduction

Diabetes is a progressive disease in which the risks of myocardial infarction, stroke, microvascular events, and mortality are all strongly associated with hyperglycemia1. Diabetes causes long term dysfunction of various organs like heart, kidneys, eyes, nerves and blood vessels. Among the various types of diabetes type 2 is the most common form affecting approximately 90 to 95 percent of diabetics worldwide and accounts for most of the public health burden attributable to diabetes2, 3.Many pathogenic processes are involved in the development of diabetes. These processes range from autoimmune destruction of the cells of the pancreas with consequent insulin deficiency to abnormalities which result in resistance to action of insulin. The basis of the abnormalities in carbohydrate, protein metabolism and fat in diabetes is deficient action of insulin on target tissues. Deficient insulin action usually results from inadequate insulin secretion and or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Defects in insulin action and impairment of insulin secretion frequently coexist in the same patient, and it is even often unclear which abnormality, if either alone, is the primary cause of hyperglycemia. Symptoms of marked hyperglycemia include polydipsia, polyuria, weight loss, sometimes with blurred vision and polyphagia, Susceptibility to certain infections and impairment of growth may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are non ketotic hyperosmolar syndrome or hyperglycemia with ketoacidosis. Long-term complications of diabetes usually include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints; and autonomic neuropathy causing genitourinary, gastrointestinal, cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased atherosclerotic cardiovascular incidence, peripheral arterial, and cerebrovascular disease. Hypertension and abnormalities of lipoprotein metabolism are mostly

found in people with diabetes4,5,6Once high-risk patients are identified, those patients who are adherent to a program of 30 min of moderate physical activity per day and get weight loss of 5–10% of initial body weight can usually expect that risk for type 2 diabetes will be reduced by at least around 50% relative to patients who are not following a therapeutic lifestyle program7. Uric acid is the end product of purine metabolism. Xanthine oxidase catalyzes the oxidation of xanthine and hypoxanthine into uric acid, producing $O_2$ and $H_2O_2$ as a by-product. Serum urate levels vary with age and sex. Most children usually have serum urate concentrations of 3.0 to 4.0 mg/dl (180 to 240 μmol/l). Levels usually begin to rise in males during teenage years but remain low down in females until menopause. Mean serum urate values of adult men and premenopausal women are 6.8 and 6.0 mg/dl (415 and 360 μmol/L), respectively. After menopause, values for women increase to near those of men. In adulthood, concentrations rise gradually over time and differ with body weight, height, blood pressure, renal function8,9and alcohol intake. Several epidemiological studies have reported that high serum levels of uric acid are strongly associated with prevalent health conditions such as obesity, insulin resistance, metabolic syndrome and diabetes, essential hypertension, and renal disease10. In recent decades, serum uric acid has emerged as a potential risk factor for type 2 diabetes mellitus (T2DM). The role of uric acid in abnormal carbohydrate metabolism also remains uncertain. It is not clear that uric acid is causative of insulin resistance or beta cell secretory deficiency, or is it a byproduct of insulin resistance or hyperglycemia. This is an important question because if uric acid is causal, then lowering down high serum uric acid levels may be a aim for early intervention utilizing antihyperuricemic agents already readily available in the market. If uric acid is just a by product of impaired glucose metabolism, it may still be useful as an early marker of T2DM risk and guide to earlier interventions, but not by treating hyperuricemia. Hyperinsulinemia has been shown to cause hyperuricemia.There are hypothesis that high uric acid is simply a byproduct of insulin resistance and glucose metabolism dysfunction11,12. However, serum uric acid levels may also mediate this syndrome. High serum levels of uric acid are also strongly associated with prevalent health conditions such as obesity, metabolic syndrome, essential hypertension and renal disease. Hyperuricemia is an independent risk factor for cardiovascular diseases.

## II. Material And Methods

**Materials of Study**

A prospective study was conducted on the patient diagnosed as diabetes mellitus type 2 visiting MMIMSR, Mullana, Ambala to estimate the serum uric acid levels. Sample size was of 500 patients selected from indoor and OPD basis during Oct 2013 to Dec 2015. Written informed consent was taken from each patient. Detailed history was be taken. General Physical examination, detailed systemic examination and investigations were carried out:

**Inclusion criteria**

1. Individuals in the age group 30-70 years suffering from type 2 diabetes mellitus, which is defined as fasting glucose concentration $\geq$ 126mg/dl.
2. Includes both men and women.
3. Diagnosed type 2 diabetes mellitus patients taking oral hypoglycaemic medications or insulin for treatment.

**Exclusion criteria**

- Individuals having type 1 diabetes mellitus.
- Diagnosed hypertensive individuals.
- Individuals known to have cardiovascular disease.
- Individuals who had cerebrovascular disease.
- Patient with pre existing renal disease.
- Individuals diagnosed as suffering from gout.
- Patients on drugs which alters serum uric acid levels.(diuretics, levodopa, pyrazinamide.)
- All other conditions which increase or decrease serum uric acid levels.

Patients of type 2 Diabetes mellitus were diagnosed on the basis of the following feature:

1. Development of disease in middle or late adult years
2. Most of the patients being obese
3. Gradual onset of symptoms
4. May be asymptomatic for many years
5. Ketoacidosis seldom occurring.
6. FBS: >126mg/dl
7. 2 hr Poast prandial blood sugar: >200mg/dl

**Investigations**

a) Complete blood counts
b) Blood sugar- fasting
c) Blood sugar-PP
d) Renal function test
e) Liver function test
f) Urine routine and microscopy
g) Glucose tolerance test (where ever necessary)
h) HbA1c (where ever necessary)
i) Estimation of Serum Uric acid level by uricase method.

## III. Observations And Results

The observations hence made have been tabulated and presented as follows.

**Table I:** Distribution of diabetic patients according to their age and gender

| Age Category | | Gender | | Total |
|---|---|---|---|---|
| | | Male | Female | |
| 30 to 39 | N | 21 | 16 | 37 |
| | % | 7.8% | 7.0% | 7.4% |
| 40 to 59 | N | 122 | 111 | 233 |
| | % | 45.2% | 48.3% | 46.6% |
| =>60 | N | 127 | 103 | 230 |
| | % | 47.0% | 44.8% | 46.0% |
| Total | N | 270 | 230 | 500 |
| | % | 100.0% | 100.0% | 100.0% |

Among the male patients only 47% were above 60 years of age group, followed by 45.2% patients who were in the age group between 40-59 years. Only 7.8% were in age category of 30-39 years.
Forty eight percent females were in the 40-59 years of age group. Only 7% of the females were in the age group of 30-39 years.

**Table 2:** Mean values for various biochemical parameters of diabetic patients

| Parameters | N | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|---|
| **FBS** | 500 | 116.00 mg/dl | 222.00 mg/dl | 144.09 mg/dl | 14.82 |
| **RBS** | 500 | 200.00 mg/dl | 450.00 mg/dl | 273.91 mg/dl | 32.59 |
| **SUA** | 500 | 2.50 mg/dl | 7.80 mg/dl | 3.96 mg/dl | 0.85 |
| **HbA1c** | 499 | 6.00% | 10.00% | 8.02% | 0.92 |

Fasting blood sugar (FBS) of patients in the present study ranged from 116.00 mg/dl to 222.00 mg/dl. Mean fasting blood sugar (FBS) of patients was 144.09±14.82mg/dl.Random blood sugar (RBS) of patients ranged from 200.00 mg/dl to 450.00 mg/dl. Mean random blood sugar (RBS) of patients was 273.91 ± 32.59mg/dl.Serum uric acid (SUA)of patients ranged from 2.50 mg/dl to 7.80 mg/dl. Mean serum uric acid was 3.96 ± 0.85mg/dl. HbA1c of patients ranged from 6.00%to 10.00%. Mean HbA1C of patients was 8.02 ±0.92%.

**Table 3:** Genderwise distribution of diabetic patients for various parameters

| Parameters | Sex | N | Mean | SD | SEM | P value |
|---|---|---|---|---|---|---|
| Age | Male | 270 | 57.17 yr | 13.66 | 0.83 | 0.218 |
| | Female | 230 | 55.73 yr | 12.03 | 0.79 | |
| FBS | Male | 270 | 145.14 mg/dl | 15.67 | 0.95 | 0.085 |
| | Female | 230 | 142.85 mg/dl | 13.70 | 0.90 | |
| RBS | Male | 270 | 273.98 mg/dl | 31.84 | 1.93 | 0.960 |
| | Female | 230 | 273.83 mg/dl | 33.52 | 2.21 | |
| SUA | Male | 270 | 3.98 mg/dl | 0.82 | 0.05 | 0.541 |
| | Female | 230 | 3.93 mg/dl | 0.89 | 0.05 | |
| HbA1c | Male | 29 | 6.31 % | 0.35 | 0.06 | 0.508 |
| | Female | 27 | 6.25% | 0.45 | 0.08 | |

Mean age of the male patients was 57.17 yr whereas mean age of the female patients was 55.73 yr .This difference is found to be non significant (p=0.218)Mean FBS of the male patients was 145.14 mg/dl whereas mean FBS of the female patients was 142.85 mg/dl. This difference was found to be statistically insignificant (p=0.085)Mean RBS of the male patients was 273.98 mg/dl whereas mean RBS of the female patients was 273.83 mg/dl. This difference was found to be statistically insignificant (p=0.960)Mean serum uric acid of the male patients was 3.98 mg/dl whereas mean uric acid of the female patients was 3.93 mg/dl. This difference was

found to be statistically insignificant (p=0.541)Mean HbAIc of the male patients was 8.31 % whereas mean HbAIc of the female patients was 8.25%. This difference was found to be statistically insignificant (p=0.508)

**Table 4:** Correlation of SUA, HbA1c and BMI in age category 30 to 39 years and 40 to 59 years of diabetic patients

| | Age Cat | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| **SUA** | 30 to 39 | 37 | 4.09 | 1.09 | 0.1796 |
| | 40 to 59 | 233 | 4.02 | 0.86 | 0.0568 |
| **HbA1c** | 30 to 39 | 37 | 8.08 | 1.03 | 0.1699 |
| | 40 to 59 | 233 | 7.97 | 0.94 | 0.0620 |
| **BMI** | 30 to 39 | 37 | 26.41 | 2.69 | 0.443 |
| | 40 to 59 | 233 | 26.82 | 3.13 | 0.205 |

Mean serum uric acid (SUA) of the patients of the age group 30 to 39 years was 4.09± 1.09 mg/dl whereas mean uric acid of the patients of the age group 40 to 59 years was 4.02 ± 0.86 mg/dl. Mean HbA1c of the patients of the age group30 to 39 years was 8.08±1.03% whereas mean HbA1c of the patients of the age group 40 to 59 years was 7.97± 0.94 %.Mean BMI of the patients of the age group30 to 39 years was 26.41± 2.69 whereas mean BMI of the patients of the age group 40 to 59 years was 26.82± 3.13.

**Table 5:** Correlation of SUA, HbA1c and BMI in age category 40 to 59 years and more than 60 years of diabetic patients

| | Age Cat | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| **SUA** | 40 to 59 | 233 | 4.02 | 0.86 | 0.0568 |
| | => 60 | 230 | 3.88 | 0.80 | 0.0531 |
| **HbA1c** | 40 to 59 | 233 | 7.97 | 0.94 | 0.0620 |
| | => 60 | 229 | 8.05 | 0.89 | 0.0590 |
| **BMI** | 40 to 59 | 233 | 26.82 | 3.13 | 0.205 |
| | =>60 | 230 | 26.80 | 2.94 | 0.194 |

Mean serumuric acid (SUA) of the patients of age group 40 to 59 years was 4.02±0.86 mg/dl whereas mean uric acid of the patients ofage more than 60years was 3.88± 0.80 mg/dl. Mean HbA1c of the patients of age group 40 to 59 years was 7.97±0.94% whereas mean HbA1C of the patients ofage groupmore than 60 years was 8.05±0.89%.Mean BMI of the patients ofthe age group 40 to 59 years was 26.82± 3.13 whereas mean BMI of the patients of the age groupmore than 60 years was 26.80 ±2.94.

**Table 6:** Mean values of SUA and FBS in diabetic patients.

| | SUA | | |
|---|---|---|---|
| **FBS** | **Mean** | **N** | **SD** |
| **100-120** | 3.000 | 1 | |
| **120-140** | 4.127 | 200 | 1.0267 |
| **>=140** | 3.860 | 299 | 0.7069 |
| **Total** | **3.965** | **500** | **0.8590** |

Mean serum uric acid (SUA) values were highest for the FBS group 120-140 mg/dl. It was lowest (3 mg/dl) when the FBS was ranging from 100-120 mg/dl.

**Table7:** Correlation between FBS and SUA in diabetic patients

| | | SUA | FBS |
|---|---|---|---|
| **SUA** | Pearson Correlation | 1 | -.114* |
| | Sig. (2-tailed) | | .011 |
| | N | 500 | 500 |
| **FBS** | Pearson Correlation | -.114* | 1 |
| | Sig. (2-tailed) | .011 | |
| | N | 500 | 500 |

Results showed that strength of association between the FBS andserum uric acid(SUA) is high and they are negatively correlated (r = -0.114).Results are statistically not significant.(p>0.01)

**Table 8:** Mean value of SUA and RBS in diabetic patients.

| RBS | SUA | | |
|---|---|---|---|
| | **Mean** | **N** | **SD** |
| **200-220** | 4.607 | 45 | 1.5358 |
| **221-240** | 3.950 | 2 | 0.0707 |
| **241-260** | 3.923 | 106 | 0.8298 |
| **>260** | 3.894 | 347 | 0.7043 |
| **Total** | **3.965** | **500** | **0.8590** |

Mean value of serum uric acid (SUA)is maximum i.e 4.60 mg/dl in the RBS group ranging from 200-220 mg/dl. The mean value of serum uric acid is lower in the other RBS groups i.e. 221-240,241-260 mg/dl and thereafter.

**Table 9:** Correlation between RBS andSUA in diabetic patients.

| | | SUA | RBS |
|---|---|---|---|
| **SUA** | Pearson Correlation | 1 | -.186** |
| | Sig. (2-tailed) | | .000 |
| | N | 500 | 500 |
| **RBS** | Pearson Correlation | -.186** | 1 |
| | Sig. (2-tailed) | .000 | |
| | N | 500 | 500 |

Results showed that strength of association between the serum uric acid (SUA) and RBS is high and they are negatively correlated (r = -0.186).Results are statistically highly significant (p<0.01).

**Table 10:** Mean value ofSUA and HbA1c in diabetic patients.

| HbA1c | SUA | | |
|---|---|---|---|
| | **Mean** | **N** | **SD** |
| **<7%** | 4.472 | 54 | 1.4418 |
| **7-8%** | 3.975 | 132 | 0.8088 |
| **8-9%** | 3.914 | 188 | 0.7130 |
| **>=9%** | 3.820 | 126 | 0.6922 |
| **Total** | **3.967** | **500** | **0.8587** |

Mean value of serum uric acid (SUA) is highest (4.472 mg/dl) if the HbA1c values are less than 7%. It is lower in other HbA1c groups i.e. 7-8 %, 8-9% and more than 9%.

**Table 11:** Correlation between SUA and HbA1c

| | | SUA | HbA1c |
|---|---|---|---|
| **SUA** | Pearson Correlation | 1 | -0.189 |
| | Sig. (2-tailed) | | .000 |
| | N | 500 | 499 |
| **HbA1c** | Pearson Correlation | -0.189 | 1 |
| | Sig. (2-tailed) | .000 | |
| | N | 500 | 500 |

Results showed that strength of association between the serum uric acid and HbA1cis high and they are negatively correlated (r = -0.189).Results are statistically highly significant (p<0.01).

**Table 12:** Correlation between SUA and BMI

| | | SUA | BMI |
|---|---|---|---|
| **SUA** | Pearson Correlation | 1 | 0.080 |
| | Sig. (2-tailed) | | 0.073 |
| | N | 500 | 500 |
| **BMI** | Pearson Correlation | 0.080 | 1 |
| | Sig. (2-tailed) | 0.073 | |
| | N | 500 | 500 |

Results showed that strength of association between the serum uric acid (SUA) and BMI is high and they are positively correlated (r = 0.080). Results are not statistically significant (p>0.01).

## IV. Discussion

In this study we found that inverse relationship between diabetes mellitus and increasing serum uric acid levels was consistently present among men (3.98 mg/dl) and women (3.93 mg/dl); however, the relationship was stronger in men. We found that SUA concentration raised with increasing fasting plasma levels up to the level of

140 mg/dl, but remarkably decreased when fasting plasma levels over 140 mg/dl. An increasing trend in the SUA concentration at the 2hPG of 220 mg/dl and a decreasing trend thereafter was also observed and an incresing trend up to HbA1c 7% and decreasing trend thereafter was noted. This observation was supported by Nan H[13] et al 2010.Very few studies have evaluated the association between 2hPG and UA due to the fact that two-hour OGTTs have not been widely applied. In study by Hodge et al[14] it was reported that SUA was strongly related with 2hPG in diabetic Mauritian men and women ($p<0.001$ for both). In the current study we have reported that the UA-2hPG association seems stronger in men and women both.Our results showed that Uric acid was inversely related with FBS($r = -0.114$), RBS($r = -0.186$), HbA1c ($r = -0.0189$). Results also showed that SUA was positively related to BMI($r =0.080$). All these observations are supported by findings in study carried out by Bandaru et al 2011[15].The are studies like Oda et al[16] and Nan et al[13]which reported that SUA is inversely related with DM. Most of these studies were partial by less sample sizes, including either women or men and not both, were from selected populations such as industrial workers or not having data on confounding factors as opposed to general population samples. A reasonable mechanism for the observed results of an inverse relationship between increasing SUA and diabetes mellitus may be related to the uric acid inhibition, reabsorption in the proximal tubule by high glucose levels in diabetic patients[17,18].

In our study in 270 Indian men and 230 Indian women, serum UA was negatively associated with diabetes in both sexes which is contrary to study by Oda et al in which they found that serum UA was positively associated with metabolic syndrome but negatively associated with diabetes in men, not in women. Epidemiologicallyand pathologically, it has been shown that decreased SUA concentration is correlated with FBS, RBS and HbA1C which are typically taken to be diagnostic criteria for type 2 diabetes. So, it is promising to establish observed positive association between risk of type 2 diabetes and decreased SUA level. Therefore, the results of this study strongly suggest and recommend that SUA can be an independent predictor of the development of type 2 diabetes. This study has some limitations. The participant's average age was 56.51 years at baseline so the role of uric acid in predicting incident of type 2 diabetes among younger adults needs further study. Because of the less number of new type 2 diabetes cases, this study had limited power for excluding complete effectiveness of uric acid prediction among IGT and normoglycemia groups. This does not unclear the main result, screening that UA adds to the prediction of type 2 diabetes among adults having IFG. This study did not incline some potential confounder like race-ethnicity, education, smoking, alcohol intake physical activity level,hypertension, and levels of glucose, cholesterol, creatinine and triglycerides.

## V. Conclusion

Five hundred patients between age 30-70 years of age of either sex, clinically diagnosed case of type 2 diabetes mellitus were included in the study.

1. Age of the patients ranged from 30-70 years. The mean age of patients was 56.51±12.95 years.
2. Male patients were 54% and females were 46%.
3. Patients in age category 40 to 59 were 233 (46.6%) and 230 (46%) in more than or equal to 60 years and 37 (7.4%) patients were in the age group 30 to 39 years.
4. Mean fasting blood sugar (FBS), random blood sugar (RBS), uric acid, HbA1cof patients were144.09±14.82mg/dl,273.91 ± 32.59mg/dl.,3.96 ±0.85mg/dl and8.02 ±0.92% respectively.
5. Mean value of serum uric acid is highest (4.472 mg/dl) if the HbA1c values are less than 7%. It is lower in other HbA1c groups i.e. 7-8 %,8-9% and more than 9%.
6. Study established the pattern of relationship between FBS, RBS, SUA in patient of diabetes mellitus for both men and women.
7. Strength of association between the FBS($r = -0.114$), RBS($r = -0.186$), HbAIc ($r = -0.189$) and serum uric acid is high and they are negatively correlated or inversely related to FBS, RBS and HbAIc
8. Strength of association between BMI ($r = 0.080$) and serum uric acid is not statisticaly significant.

It is thus concluded that serum uric acid in patients of diabetes mellitus type 2 is inversely related to FBS, RBS and HbA1c. Therefore serum uric acid (SUA) levels might act as predictor and prognostic marker of diabetes mellitus type 2 but its clinical implication need to be further studied.

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