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Relationship between serum uric acid levels and glycaemic control in patients of type 2 Diabetes Mellitus.

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Abstract

Variations in uric acid levels have been increasingly associated with insulin resistance, hyperinsulinemia and diabetes. So the present study was undertaken to evaluate serum uric acid levels in patients of type 2 diabetes mellitus. It was a case control study. The subjects included in the study were divided into 2 groups – controls and patients. Based on the $HbA1_c$ levels patients are further sub divided. Serum levels of fasting blood sugar, $HbA1_{c,}$ serum uric acid, BUN and serum creatinine were estimated in all the subjects. The results were compared and represented as mean and standard deviation. One way analysis of variance (ANOVA) has been used for statistical analysis and comparison of parameters between different groups. Present study concludes that serum uric acid levels increased with moderately increasing levels of HbA1c<7% and then decreased with further increasing levels of $HbA1_c$>7%.

Key Words: Type 2 Diabetes Mellitus, $HbA1_{c,}$ serum uric acid, fasting blood sugar.

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Introduction

Diabetes Mellitus is a cluster of abnormal paradigm having a common feature of hyperglycaemia [1]. Being a chronic metabolic disorder, it has assumed epidemic proportion and its long term complications can have devastating consequences [2]. The long term control of diabetes mellitus (DM) is judged by glycated hemoglobin which was first isolated by Allen et al [3].

The uric acid is the end product of purine metabolism in human. Plasma uric acid is found to be raised in many patients of Diabetes Mellitus. Elevation of serum uric acid has been found to be associated with subsequent morbidity and mortality in the general population among patients with congestive heart failure, diabetes and hypertension [4]. Increased levels of uric acid in patients of type 2 DM

could be due to increased levels of serum Adenosine Deaminase, an enzyme which is responsible for converting adenosine to uric acid [5, 6].

Not much data is available on the relationship of serum uric acid with type 2 DM , so the present study was undertaken to find any correlation of serum uric acid with the glycaemic control in patients of type 2 DM.

Material and methods

The subjects included in the present study were 60 patients of Type 2 diabetes mellitus in age group of 40-65 years of either sex, on oral hypoglycaemic drugs, attending the OPD of Department of Medicine of the institute. A group of 30 normal healthy individuals, age and sex matched from the same population served as controls.

These 90 subjects were divided into 3 groups:

- GROUP A comprised of 30 normal healthy individuals who volunteered for getting included in the present study.
- GROUP B comprised of 30 patients of Type 2 Diabetes Mellitus on oral hypoglycaemic drugs with $HbA1_c$<7%.
- GROUP C comprised of 30 patients of Type 2 Diabetes Mellitus on oral hypoglycaemic drugs with $HbA1_c$>7%.

All the patients and the controls were from the same population in the age group of 40–65 years of either sex. Informed consent was taken from all the subjects included in the study. Patients with type 1 diabetes mellitus, acute complications of diabetes mellitus and history of acute infection or other ailments like gross congestive heart failure, tuberculosis, gout, rheumatoid arthritis, skeletal muscle injury and renal failure were not included in this study.

It was a case control prospective study. A complete clinical examination of subjects was done. The subjects were screened for fasting blood sugar (FBS), serum uric acid, glycated haemoglobin, serum creatinine and blood urea nitrogen (BUN). Fasting blood sugar estimation by GOD-POD Method [7]. Glycated hemoglobin ($HbA1_c$) estimation was done by Nycocard Reader [8]. Serum uric acid estimation by Trivedi R.C. et al [9]. Serum creatinine estimation by Jaffe kinetic method as described by Bartel [10] and BUN estimation by GLDH-Urease Method by Tiffany [11].

Statistics: Results were analyzed by Oneway ANOVA and Post Hoc Turkey HSD and a probability of less than 5% ($p<0.05$) was considered to be statistically significant. The study was approved by the ethical committee of the institute.

Results

The statistical analysis showed sex and number distribution in these three groups was comparable. (Table -1)

Table -1: Showing sex and number distribution in the three groups

M- Male, F- Female

	Group A	Group B	Group C
Number	30	30	30
M / F (% age)	53.33/46.66	70/30	43.33/56.66

The mean values of BUN in Group A were 14.31± 11.47 mg/dl, in Group B were 15.10± 7.80 mg/dl and in Group C were 14.38± 8.94 mg/dl. The difference was statistically not significant among the three groups ($p>0.05$). (Table-2)

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Group	N	Range (mg/dl)	Mean ± SD (mg/dl)	95% CI	Comparison	P value
Group A	30	6 – 68	14.31± 11.47	10.02-18.59	Group A vs. B	0.944^{NS}
Group B	30	3 – 27	15.10± 7.80	12.19-18.01	Group B vs. C	0.954^{NS}
Group C	30	3 – 39	14.38± 8.94	11.04-17.72	Group A vs. C	0.999^{NS}

Table – 2: Comparison of Blood Urea nitrogen (BUN) in the three groups.

N: Number of cases; SD: Standard Deviation; CI: Confidence Interval; NS: p>0.05, Not Significant.

Group	N	Range (mg/dl)	Mean ± SD (mg/dl)	95% CI	Comparison	P value
Group A	30	0.6 - 1.6	1.07± 0.22	0.99-1.15	Group A vs. B	0.662^{NS}
Group B	30	0.5 – 1.9	0.995± 0.39	0.85-1.14	Group B vs. C	0.236^{NS}
Group C	30	0.5 – 1.9	1.14± 0.37	0.997-1.28	Group A vs. C	0.723^{NS}

Table – 3: Comparison of Serum Creatinine in the three groups

The mean values of creatinine in Group A were 1.07± 0.22 mg/dl, in Group B were 0.995± 0.39 mg/dl and in Group C were 1.14± 0.37 mg/dl. The difference was statistically not significant among the three groups (p>0.05). (Table -3)

The mean FBS levels of Group A were 82.00± 13.00 mg/dl, Group B were 126.12± 22.71 mg/dl and the corresponding values among Group C subjects were 136.97± 24.88 mg/dl. In the present study, the mean FBS levels of Group B and Group C were found to be highly significantly higher than Group A (p <0.001). Although the mean FBS levels of Group C were higher than Group B but the difference was statistically not significant (p=0.115). It was further observed that the mean $HbA1_c$ levels in Group A were 5.75± 0.46%, in Group B were 6.09± 0.56% and the corresponding values among Group C were 8.72± 1.35%. From this study it was observed that the difference in the levels of $HbA1_c$ was found to be insignificant between Group B and Group A (p= 0.300). (Table -4)

Table – 4: Showing FBS & HbA1c in control and study groups

Group	No.	FBS			$HbA1_c$		
		Mean ± SD	Comparison	P value	Mean ± SD	Comparison	P value
Group A	30	82.00± 13.00	Group A vs. B	<0.001***	5.75± 0.46	Group A vs. B	0.300^{NS}
Group B	30	126.12±22.71	Group B vs. C	0.115^{NS}	6.09± 0.56	Group B vs. C	<0.001***
Group C	**30**	**136.97± 24.88**	**Group A vs. C**	**<0.001*** **	**8.72± 1.35**	**Group A vs. C**	**<0.001*** **

No.: Number of cases; SD: Standard Deviation; p < 0.001 Highly Significant

The mean serum uric acid levels in Group A were 6.34± 1.62 mg/dl, in Group B were 6.90± 1.90 mg/dl and in Group C were 5.13± 1.32 mg/dl. The mean serum uric acid levels of Group B were significantly higher than Group C (p<0.001) whereas levels of mean serum uric acid in Group C were significantly lower than Group A (p=0.014) but no significant difference was observed between Group A and Group B (p=0.381). (Table- 5)

Group	N	Range (mg/dl)	Mean ± SD (mg/dl)	95% CI	Comparison	P value
Group A	30	3.8-9.3	6.34 ± 1.62	5.74-6.95	Group A vs. B	0.381^{NS}
Group B	30	4.2-12.9	6.90 ± 1.90	6.19-7.61	Group B vs. C	<0.001***
Group C	30	3.3-7.5	5.13 ± 1.32	4.64-5.63	Group A vs. C	0.014*

Table – 5: Comparison of Serum Uric acid levels in the three groups

CI: Confidence Interval; NS: p>0.05 Not Significant; *P< 0.05 Significant at 5% significance level; ***P<0.001 Highly Significant

The Pearson's correlation coefficient for the relationships between Uric acid and $HbA1_c$ levels in Group B showed positive correlation (r=0.196). (Table-6)

The Pearson's correlation coefficient for the relationships between Uric acid and $HbA1_c$ levels in Group C showed negative correlation (r= -0.015).

Discussion

Alterations in serum uric acid levels associated with the full range of glucose intolerance are not uniform. While impaired glucose tolerance is accompanied by elevated serum uric acid, overt diabetes is reported to be

associated with low levels in the absence of nephropathy [12, 13].

In the present study the mean serum uric acid levels of Group B were significantly higher than Group C ($p<0.001$) whereas levels of mean serum uric acid in Group C were significantly lower than Group A ($p=0.014$). Although the mean serum uric acid levels of Group B were higher than Group A, but the difference was not statistically significant ($p=0.381$). Thus suggesting that there is increased uric acid levels in patients with $HbA1_c$ <7% and decreased uric acid levels in patients with $HbA1_c$ >7%. (Table - 5)

The Pearson's correlation coefficient for the relationships between Uric acid and $HbA1_c$ levels in Group B showed positive correlation ($r=0.196$) which was statistically not significant ($p=0.300$) **Table-6, Fig-1a.** The reason for increased uric acid levels could be due to increased activity of ADA, an enzyme responsible for converting adenosine to uric acid in patients of type 2 Diabetes Mellitus [5]. Another reason behind the increase in serum uric acid levels could be due to increased flux of glucose-6-phosphate through the hexose monophosphate shunt due to impairment of the glycolytic pathway. This finding was in accordance with study by Modan M et al [14].

Parameter		Group B	Group C
		$HbA1_c$	$HbA1_c$
Uric acid	r value	.196	-0.015
	p value	.300	.939

Table– 6: Comparison of Serum Uric acid and $HbA1_c$ in Group B and Group C

r value : Pearson correlation coefficient; *. Correlation is significant at the 0.05 level; **. Correlation is significant at the 0.01 level.

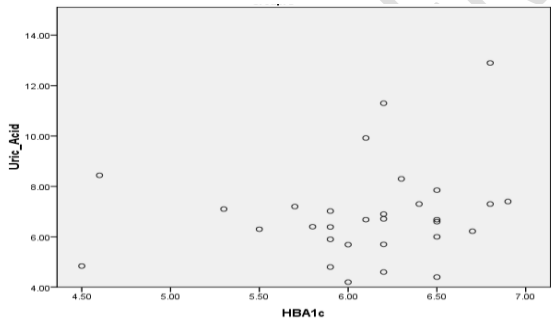

Fig-1a: Correlation between $HbA1_C$, and Uric Acid in Group B

The Pearson's correlation coefficient for the relationships between Uric acid and $HbA1_c$ levels in Group C showed negative correlation ($r=-0.015$) which was statistically not significant ($p=0.939$) suggesting thereby that when the levels of $HbA1_c$ increased more than 7% there is decrease in uric acid levels **Table-6 Fig-1b**. The reason for this finding is thought to be due to the uricosuric effect of glycosuria. This finding was in accordance with Choi HK et al [15] and Tuomilehto J et al study [16].

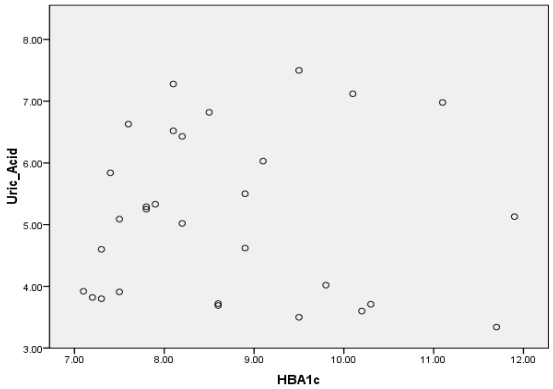

Fig. 1 b: Correlation between $HbA1_C$, and Uric Acid in Group C

Conclusion

This study suggests that the serum uric acid levels increased with moderately increasing levels of $HbA1_c$ (<7%) and then decreased with further increasing levels of $HbA1_c$ >7% showing a bell-shaped relationship. Individuals with overt diabetes are at a lower future risk of gout independent of other risk factors.

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