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Serum uric acid serve as a potential biomarker of deterioration of glucose metabolism. A cross-sectional study done in Zoram medical college, FALKAWN Mizoram, India.

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ABSTRACT

Background and aims: With the deepening of the researches on uric acid, especially in the study of metabolic diseases, uric acid has been found to be closely related with diabetes. Uric acid cause a series of pathophysiological changes through inflammation, oxidative stress, vascular endothelial injury, and so on and thus subsequently promotes the occurrence and development of diseases. The objective of the study is to estimate uric acid level and its relation with diabetes, biomarker for deterioration of glucose metabolism. **Methods**: A cross-sectional study with subgroup analysis, 60 cases and 60 patients with complication. Fasting blood sugar (FBS), Post prandial blood sugar (PPBS), GlycatedHb (HbA1c) were also measured. **Results**: Thus, out of 60 cases have high uric acid level which is found to be significant with p value (<0.009). **Conclusion**: Uric acid levels have tendency to decrease in early course of disease and tends to increase with onset of complications. Thus, a preventive, cost-effective approach is available with potential implications for public health.

Keywords: Uric acid, metabolic diseases, glucose metabolism, oxidativestress, fasting blood sugar.

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Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. Associated metabolic dysregulation causes secondary pathophysiologic changes in multiple systems that impose a tremendous burden on the individual and on the health care system.

WHO projects ~ 300 million diabetic patients worldwide by 2025 with the greatest number expected in China and India.Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.Associated metabolic dysregulation causes secondary pathophysiologic changes in multiple systems that impose a tremendous burden on the individual and on the health care system.

WHO projects ~ 300 million diabetic patients worldwide by 2025 with the greatest number expected in China and India.Higher insulin levels can reduce renal excretion of uric acid as insulin can stimulate the urate anion exchanger or the Na^+ dependent anion co transporter in brush border membranes of the proximal tubule and increase renal urate reabsorption.However, serum uric acid is significantly independent of confounders early in the course of diabetes but associated with later development of persistent macroalbuminuria.Therefore, uric acid may be a novel and important player in the pathogenesis of microvascular complications of diabetes. The relationship between uric acid and diabetes has gradually become a hot topic of research. On the one hand, some study reported uric acid was not associated with diabetes. On the opposite hand, more clinical trials demonstrated uric acid was significantly associated with diabetes. Though reading a large number of literature and studies, we believe that uric acid is closely related to diabetes. Poor lipid metabolism in individuals with higher uric acid levels may lead to increased fasting and postprandial insulin levels, high-sensitivity C-reactive protein, hepatic insulin resistance index and decreased glomerular filtration rate and skeletal muscle insulin sensitivity and insulin clearance. Diabetic microangiopathy refers to atherosclerosis of blood vessels such as aorta, coronary artery, renal artery which is caused by dysfunction of endothelial cells, advanced glycation end product. Diabetic neuropathy is one of the most common chronic complication of diabetes characterized by damage to nerve glial cells, axons, and endothelial cells. The pathophysiology changes conclude polyol pathway, PKC activity, increased AGEs, ROS, nerve degeneration and regrowth.

Methods

This hospital based study was started after obtaining clearance from Institute Ethics Committee (IEC) ZORAM MEDICAL COLLEGE. A cross sectional design with subgroup analysis, 60 cases and 60 controlled prospectively from outpatient department of General Medicine Department of our hospital within a time period of 12 months between March 2019- February 2020. Cases comprises of 60 diabetic patients and control comprises of 60 individuals with complications attending diabetic clinic and those admitted in general medicine ward.

Inclusion criteria

1. Adults (18-60 years) who are diabetic and are under medication
2. Willingness to participate in the study.

Exclusion criteria

1. Patients on thiazides and alcoholics
2. Malignancy and inflammatory diseases
3. Patients suffering from other renal diseases

About 5ml of fasting blood sample was drawn from all subjects after an overnight fast, also after 2 hours post prandial. The serum was separated by centrifuging the blood at 3000 rpm for 10 minutes. Serum glucose was estimated by spectrophotometric method. (AU2700 Chemistry auto-analyser, Beckman Coulter, inc.)

Written informed consent taken & sample collected

Uric acid was estimated using enzymatic colorimetric, Randox kit

HbA1c was done using Fast Ion Exchange Resin Separation Method, Human kit

Lipid profile was done by enzymatic colorimetric, Human kit.

Statistical analysis

Database was constructed in Microsoft excel 2007 and statistical analysis was done using IBM statistical package for the social sciences (SPSS 17.0).Data were expressed in percentages, mean with standard deviation.

Pearson correlation coefficient test were done to analyse the data. $p < 0.05$ was considered statistically significant.

Results

In this study, there were in total 120 participants which was sub-grouped into 60 cases DM and another 60 cases of diabetes with complications in this study.

Table 1: This table shows baseline characteristics of the study population.

Parameters		Control(n=60)	DM(n=60)	DM#C(n=60)
Age (Mean±SD)		54.21±8.59	52.83±9.08	58.68±11.20
Sex (Male,%)		51.7	48.33	60.65
Inhabitancy (%)	Urban	71.2	66.66	61.66
	Rural	28.3	33.33	38.33
Family history	Yes	41.66	58.33	51.66
	No	58.33	41.66	48.33
Duration of disease, in years		-	2.56	6.96
BMI (Mean±SD)		23.7±3.01	24.67±3.9	24.86±3.77
Blood Pressure (Mean±SD)	SBP	119.5±13.7	124.63±19.52	131.4±17.98
	DBP	73.36±12.87	77.63±13.98	80.96±13.90

Figure 1: This figures shows age wise distribution of the study group

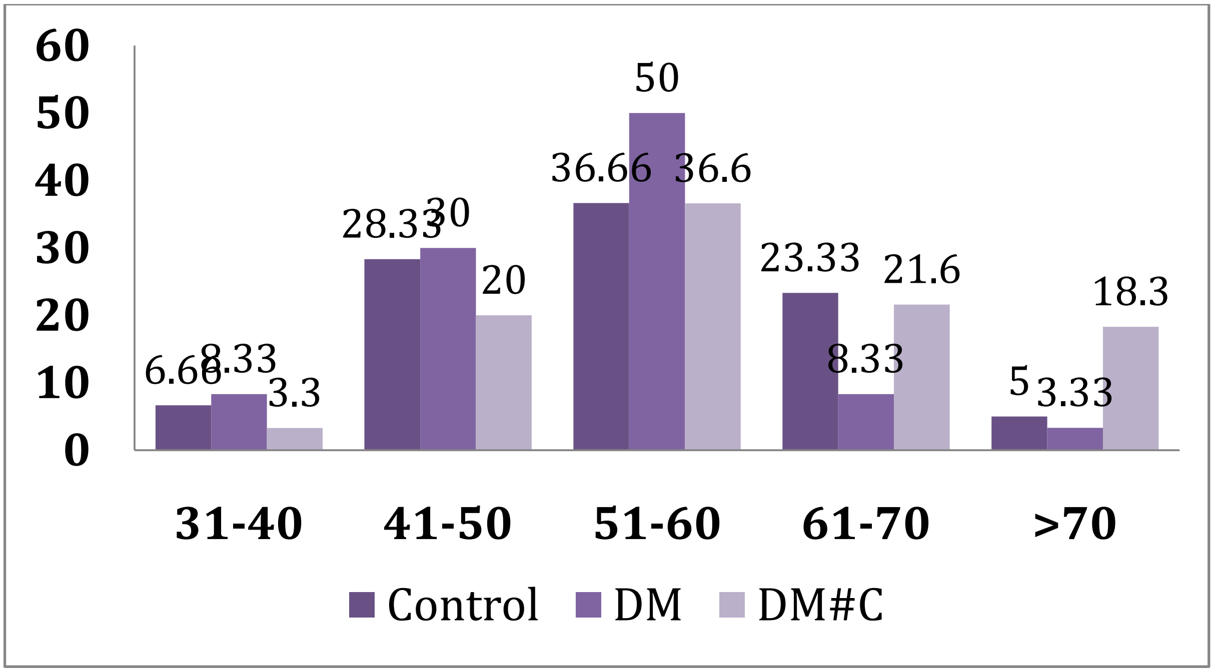

Figure2: Age wise distribution of study group

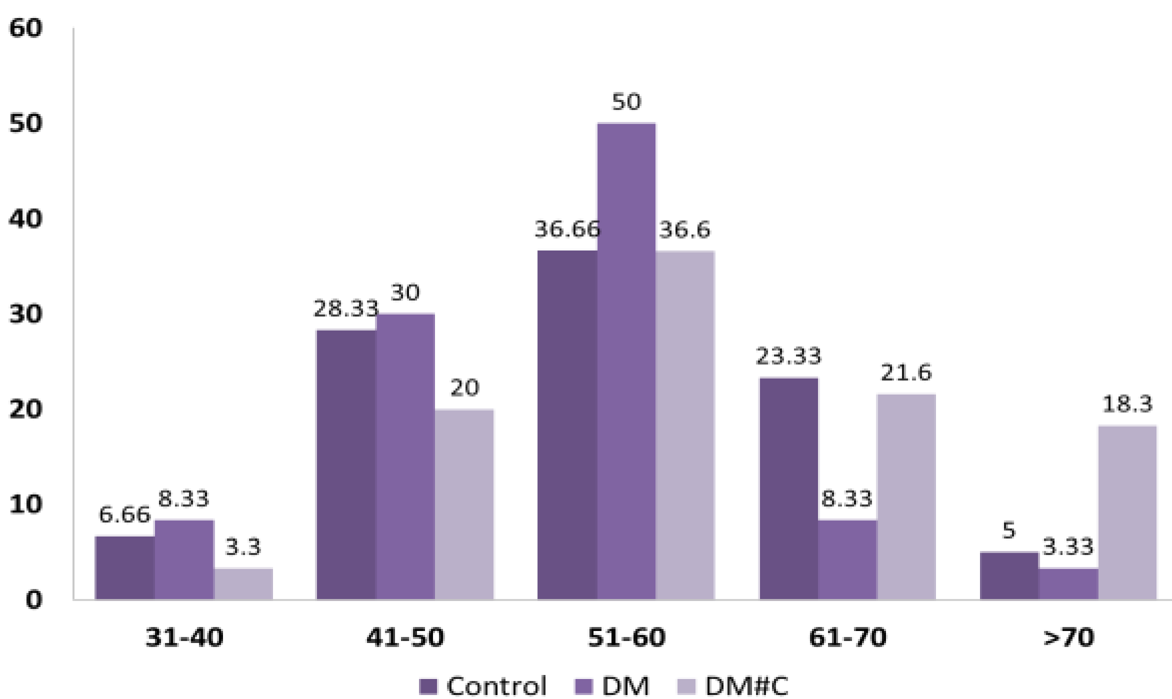

Figure 3: Distribution of diabetic cases by serum uric acid level

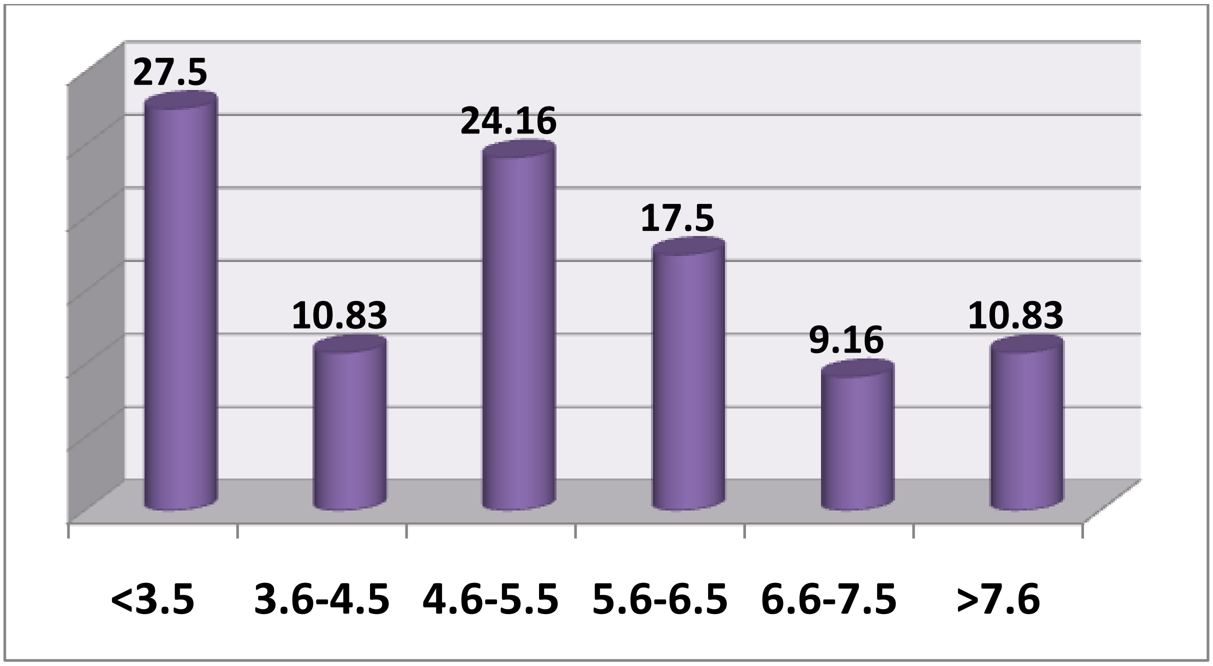

Figure 4: Distribution of diabetic cases by serum uric acid level

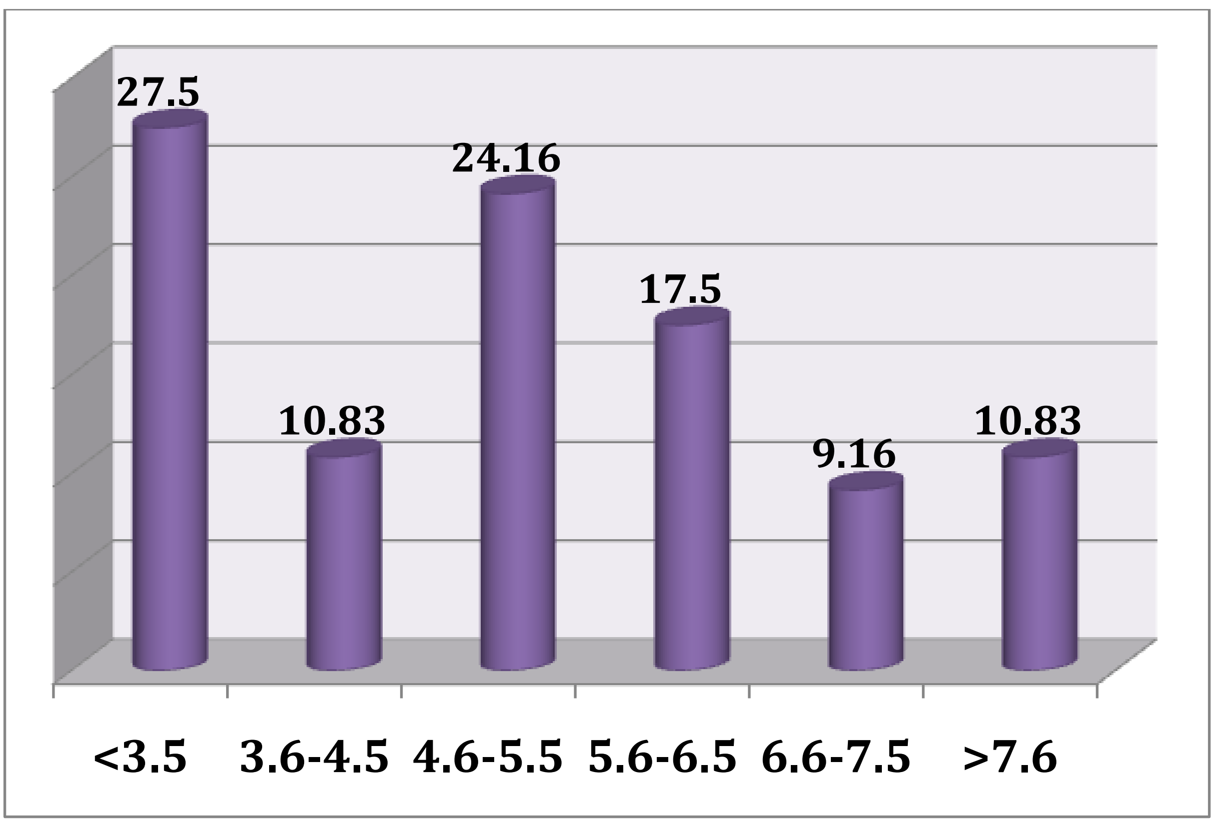

Table2: Glycemic status and distribution of diabetic cases by HbA1c levels

Glycemic status	HbA1c	Male	Female	Total No (%)
Good	<6	20	23	43 (35.83%)
Poor	6.1-9	35	29	64 (53.53)
Worst	>9.1	10	3	13 (10.83)

Table 3: Summary of biochemical parameters

Parameters	Control	DM	P-value (a)	DM#C	P-value (b)
FBS (mg/dl)	84.61±13.79	166.11±65.67	**0.001**	152.25±81.32	**0.001**
PPBS (mg/dl)	117.50±40.57	251.83±104.99	< **0.001**	246.61±94.71	< **0.001**
HbA1c (mg%)	4.07±0.74	5.77±2.01	< **0.001**	6.96±1.97	< **0.001**
Uric acid (mg/dl)	5.20±1.41	4.82±1.85	0.13	6.04±1.72	**0.009**
Urea (mg%)	21.83±8.86	33.51±13.75	< **0.001**	60.48±39.45	< **0.001**
Creatinine (mg%)	0.87±0.3	1.15±0.87	**0.048**	3.62±3.34	< **0.001**

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Discussion

Most prevalent in the middle aged population → mean age of 52.83 ± 9.08 in diabetes group and 58.68 ± 11.20 in diabetes with complication groups ***(Schulze MB et al).*** Behavior of uric acid levels in DM shown to be quite different in patients with/without complication. Mean serum uric level was lower in diabetes group as compared to control group (***Herman JB et al).***

So, the finding of low levels of uric acid in diabetes could be explained by the intermittent or constant hyperglycaemia and glycosuria experienced by diabetic subjects.

This study shows a significant increase in serum uric acid levels in diabetes with complication as compared to diabetes without complication (***Ashakiran S et al***).

Hyperglycemia with other metabolic abnormalities of diabetes e.g. insulin resistance, dyslipidemia& AGEs ~ NO production and excess production of ROS in endothelium and vascular smooth muscles promoting atherosclerosis.

Behaviour of uric acid levels may thus indicate along with coexistence of lipid derangements, the ongoing pathophysiology in diabetes in relation to glycemic control, insulin resistance, onset and progression of complications.

Serum uric acid level when categorised on the basis of gender, it was found to be lower in female as compared to male - ***Nan H et al&Conen D et al.***

Furthermore, when diabetic cases were stratified based on their HbA1c levels, it was found that with increasing HbA1c levels, the serum uric acid levels also increase - ***Choi HK et al.***

The most common microvascular complication of diabetes in the present study is nephropathy (41.66%) - ***Gomez FJC et al.***

Significant positive correlations were found between serum uric acid and duration of diabetes, diastolic blood pressure, HbA1c and triglyceride - ***Li et al.***

Conclusion

Uric acid levels have tendency to decrease in the early course of disease and tends to increase with the onset of complication. Serum uric acid may serve as a potential biomarker of deterioration of glucose metabolism.

Measurement of uric acid is easy in terms of preanalytics, can be performed with simple methods in routine laboratories, and is inexpensive. Thus, a preventive, cost effective approach is available with potential implications for public health.

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Nil

Conflicts of interest

There are no conflicts of interest

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