



## TO STUDY ROLE OF URIC ACID AS A BIOMARKER FOR INSULIN RESISTANCE IN TYPE 2 DIABETIC MELLITUS

### Biochemistry

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### ABSTRACT

**Objective:** The current study has undertaken to explore the role of uric acid as a biomarker for insulin resistance in type 2 diabetic mellitus.

**Material and Method:** The study was conducted on 100 subjects of type 2 diabetic patients in Meerut District. Serum uric acid, Fasting plasma glucose, fasting plasma insulin and HOMA- IR were analyzed.

**Result:** The study showed that there were significantly increased Serum Uric acid, Fasting Plasma Glucose, Fasting Serum Insulin and HOMA-IR values in T2DM subjects as compared to controls ( $p < 0.0001$ ).

**Conclusion:** There is convincing evidence that there were significant correlation between uric acid and HOMA-IR value. Hyperuricemia is related to risk factors for insulin resistance in type 2 diabetes. The study concluded a significant progressive relationship between increased uric acid level with respect to HOMA-IR levels which is an indices of insulin resistance.

### KEYWORDS

Homeostasis model assessment (HOMA-IR), Insulin Resistance, Type 2 Diabetic mellitus (T2DM), Uric acid (UA).

### Introduction

Type 2 diabetes is a serious and common chronic disease resulting from a complex inheritance-environment interaction along with other risk factors such as obesity and sedentary lifestyle. Type 2 diabetes and its complications constitute a major worldwide public health problem, affecting almost all populations in both developed and developing countries with high rates of diabetes-related morbidity and mortality. The prevalence of type 2 diabetes has been increasing exponentially, and a high prevalence rate has been observed in developing countries and in populations undergoing "westernization" or modernization. Hyperuricemia, the precursor of gout, is strongly associated with insulin resistance syndrome, an established risk factor for type 2 diabetes. This link may be translated into an independent association between hyperuricemia and the future risk of type 2 diabetes, but little prospective data on the topic are available, particularly in the general population. Indeed, studies of individuals with impaired glucose levels have suggested that hyperuricemia is an independent risk factor for diabetes.

Identifying risk factors for the development of type 2 diabetes is essential for its early screening and prevention. Serum uric acid (SUA) level has been suggested to be associated with risk of type 2 diabetes. Biologically, uric acid (UA) plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake. However, hyperinsulinemia as a consequence of insulin resistance causes an increase in SUA concentration by both reducing renal UA secretion and accumulating substrates for UA production. Therefore, it remains controversial whether SUA is independently associated with the development of type 2 diabetes.

The aim of our study was to examine the independent association between serum uric acid levels and the future risk of insulin resistance in type 2 diabetic mellitus.

### Material and Method

#### Material

This study was conducted during the period from the June 2016 until the end of November 2017 in Chhatrapati Shivaji Hospital, Subharti Medical College Meerut, U.P. India. A total of 100 subjects of type 2 diabetes (54 male and 46 female) having an age group of 40-65 years were participated from urban and rural area of Meerut. Patients with cardiovascular, thyroid function disorder, and other hormonal disorders that may exaggerated the insulin resistance in type 2 diabetes were excluded from the study. 5 ml of venous blood was obtained after a 12 hour fast from type 2 diabetic patients. Blood samples were transferred into tube, allowed to stand for 15 minutes at room temperature, centrifuged at 3500 rpm for 10 minutes.

### Methods

#### Determination of Serum Uric Acid

Serum uric acid levels were measured with an autoanalyzer by the

enzymatic colorimetric method (Uricase).

#### Determination of Fasting Glucose

Fasting glucose concentration was measured by the enzymatic colorimetric method (GOD-POD).

#### Determination of Fasting Insulin

Fasting insulin concentration was measured by enzyme linked immune sorbent assay (ELISA) method based on the sandwich principle.

#### Determination of Insulin Resistance

The insulin resistance was calculated by a homeostasis model assessment (HOMA-IR) index = Fasting plasma glucose (mg/dl) X Fasting plasma Insulin (uU/ml) / 405, as described by Matthews and colleagues 1985.

#### Statistical analysis:

Data analysis was performed using Epi info software version 3.5.1. Descriptive statistics, including mean, range, and standard deviations, were calculated for all variables. Proportions were compared using Chi-square tests and chi square for trend at 0.05 level of significance.

### Result

**Laboratory findings between the study groups (T2DM patients) and control group (Non – diabetic Healthy controls).** offers faster recovery, less risk of infection and minimally invasive.

Parameters	Study group (no=100) Mean ± S.D.	Control group (no=50) Mean ±S.D.	P value
Serum Uric acid (mg/dl)	6.27± 1.39	4.39 ± 1.24	p <0.0001
Fasting Plasma Glucose (mg/dl)	176.34 ± 16.79	86.13 ± 11.36	p <0.0001
Fasting Serum Insulin (µIU/ ml)	9.11 ± 1.89	6.23 ± 1.43	p <0.0001
HOMA-IR	3.87 ± 0.07	1.32 ± 0.04	p <0.0001

Table shows comparison of laboratory findings between the study groups (T2DM subjects) and control group (Non – diabetic Healthy subjects). The mean level of Serum Uric acid, Fasting Plasma Glucose, Fasting Serum Insulin and HOMA-IR in T2DM patients were 6.27 ± 1.39 mg/dl, 176.34 ± 16.79 mg/dl, 9.11 ± 1.89 µU/ml and 3.87 ± 0.07 respectively. On the other hand in controls the mean level were observed as 4.39 ± 1.24 mg/dl, 86.13 ± 11.36 mg/dl, 6.23 ± 1.43 µU/ml and 1.32 ± 0.04 respectively.

### Discussion

It is evident from results that there were significantly increased Serum Uric acid, Fasting Plasma Glucose, Fasting Serum Insulin and

HOMA-IR values in T2DM subjects as compared to controls ( $p < 0.0001$ ). Our data suggest that clearance of UA is being reduced with increase in insulin resistance and UA as a marker of diabetes period. A plausible mechanism for the observed results of an association between increasing serum uric acid and diabetes mellitus may be related to the inhibition of uric acid reabsorption in the proximal tubule by high glucose levels in diabetic individuals.

Hyperinsulinemia decreases uric acid clearance by the kidneys; the mechanism is an increased proximal tubular urate transport from the glomerular filtrate to the renal interstitium by stimulation of GLUT 9, one of its major transporters, which leads to hyperuricemia.<sup>2</sup>

Our result has shown strong links between uric acid levels and HOMA-IR, a combination of medical conditions that are related to insulin resistance (the body's inability to correctly process insulin) and increase a person's chances of getting heart disease and diabetes.

Our results agree with those of Kivity and colleagues<sup>14</sup> who found that high serum uric acid concentrations are associated with diabetes in women, but not in men, and with those from Nagahama and colleagues,<sup>15</sup> who found that although hyperuricemia is a strong predictor of metabolic syndrome in both, male and female patients, the risk was higher in women. No explanation is available for this sex difference, but the distinct fat distribution between sexes, the different levels of uric acid in men and women, and the effects of estrogens on renal clearance of urate may explain it.<sup>16,17</sup>

It has been recognized that serum uric acid (UA) is positively associated with serum glucose levels in healthy subjects. Recent studies have demonstrated that UA levels are higher in subjects with prediabetic and early Type 2 diabetes than in healthy controls. Furthermore, an elevated serum UA level was found to increase chances for developing Type 2 diabetes in individuals with impaired glucose tolerance. Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance and/or hyperinsulinemia in metabolic syndrome. An elevated UA levels, as reported, often precedes the development of obesity, hyperinsulinemia, and diabetes.

In addition, uric acid has been implicated in the development of metabolic syndrome and hypertension. However, hyperuricemia is not always found in diabetic individuals. Conflicting data exist about UA levels in Type 2 diabetes, as low levels were found in diabetic patients, while elevated serum UA is a feature of hyperinsulinemia and impaired glucose tolerance. Although several studies have implicated the role of UA in progression of prediabetic to diabetes, studies related to UA levels in diabetes development are controversial and deserve further analysis. Therefore, in this study we have analyzed and examined potential role of UA as a biomarker for impaired glucose metabolism and diabetes progression by analyzing serum levels of UA in Type 2 diabetic patients.