Interrelationship of Fasting Blood Glucose, Glycated Hemoglobin and Serum Uric Acid Levels in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and hyperglycemia. Glycemic control in diabetic individuals is commonly assessed utilizing glycated hemoglobin (HbA1c) and fasting blood glucose (FBG) levels. However, recent evidence indicates that serum uric acid (SUA), traditionally associated with gout and renal disease, and may also perform significant function in pathophysiology of T2DM and its complications. Elevated Serum uric acid has been linked with insulin resistance, oxidative stress, and inflammation—all key features of metabolic syndrome and diabetes progression.

Objectives: This study aims to assess the correlation between fasting blood glucose, glycated hemoglobin (HbA1c), and serum uric acid levels in patients diagnosed with Type 2 Diabetes Mellitus.

Materials and Methods: A cross-sectional observational study has been undertaken at a tertiary care hospital comprising 150 patients clinically diagnosed with T2DM, collected Fasting blood samples for estimation of HbA1c, plasma glucose, and serum uric acid using standard enzymatic and immunoturbidimetric methods. Correlation analysis has been undertaken utilizing Pearson's correlation coefficient for determining association between serum uric acid and glycemic markers (FBG and HbA1c).

Results: Study participants' mean age was 52.4 ± 10.7years. FBG and HbA1c exhibited highly significant positive correlation ($r=0.78$, $p<0.001$). Serum uric acid levels showed a mild to

moderate positive correlation with FBG (r=0.29, p=0.015) and HbA1c (r=0.36, p=0.002). Higher uric acid levels were notably observed in individuals with poor glycemic control (HbA1c > 8%).

Conclusion: Current study highlights a statistically significant association between SUA and established glycemic markers in T2DM. Serum uric acid, although not a conventional marker, may provide valuable insight into metabolic disturbances and glycemic control in diabetic patients. Further longitudinal and mechanistic research is warranted for examining its role in diabetes management and complication risk prediction.

Keywords: Type 2 Diabetes Mellitus, Glycated Hemoglobin, Uric Acid, Hyperuricemia, Hyperglycemia, and Fasting Blood Glucose.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) has emerged as one of the most prevalent chronic non-communicable diseases globally, posing a significant public health challenge. In 2021, International Diabetes Federation (IDF) reported that Type 2 diabetes accounted for over 90% of the cases, estimating 537 million adults worldwide living with condition. India, in particular, harbors one of the largest diabetic populations, earning it tag of the "Diabetes Capital of the World." [1] The increasing incidence is largely driven by urbanization, sedentary lifestyles, dietary transitions, genetic predisposition, and obesity. Despite advances in diagnostic and therapeutic strategies, diabetes remains associated with high risk of vascular complications and early mortality, underscoring need for comprehensive metabolic assessment and monitoring.

Type 2 diabetes is characterized by increased β-cell dysfunction and insulin resistance, resulting in chronic hyperglycemia. Persistent elevations in blood glucose levels contribute to macrovascular and microvascular complications, including cardiovascular disease, nephropathy, neuropathy, and retinopathy. To mitigate these risks, early diagnosis and sustained glycemic control are critical. Conventionally, FBG and HbA1c are widely accepted and validated tools for monitoring glycemic control. FBG reflects short-term glucose status, while HbA1c provides a retrospective view of glycemia over the past 2-3 months. [2]

Recent literature has turned attention toward other biochemical markers, such as SUA, which have traditionally been related to gout and renal dysfunction. [3] Increasing evidence indicates

that serum uric acid plays a much broader role in metabolic diseases, including obesity, hypertension, diabetes, and metabolic syndrome. Hyperuricemia has been implicated as both a cause and a consequence of insulin resistance, via mechanisms comprising low-grade inflammation, oxidative stress, endothelial dysfunction, and renal impairment. [4] Elevated SUA levels might impair nitric oxide production, reduce insulin-mediated glucose uptake, and promote pro-inflammatory cytokines—all of which exacerbate the pathophysiology of diabetes.

Relationship between SUA and glycemic indices in T2DM has generated considerable interest but remains controversial and complex. [5] Some studies report a positive correlation, suggesting that elevated SUA is associated with worsening glycemic control. Conversely, other findings point to an inverse or non-significant association, particularly in patients with advanced renal disease or long-standing diabetes. These inconsistencies may be due to variations in study populations, disease duration, comorbid conditions, or pharmacological interventions such as diuretics and antidiabetic medications. [6]

The kidneys are primarily responsible for excreting uric acid, end product of purine metabolism. [7] Hyperuricemia results from improved renal tubular reabsorption of uric acid in setting of insulin resistance. Furthermore, hyperglycemia itself may induce oxidative stress, which in turn stimulates xanthine oxidase activity and uric acid production. Inflammatory mediators, encompassing interleukin-6 (IL-6) as well as tumor necrosis factor-alpha (TNF-α), exhibiting an increase in T2DM, further modulate uric acid metabolism and contribute to endothelial injury and insulin resistance. [8,9]

This study was conceptualized in light of the growing interest in non-conventional biomarkers and the need for more comprehensive metabolic profiling in T2DM. By exploring the interrelationship between glycated hemoglobin, FBG, and SUA, we aim to evaluate whether SUA can serve as adjunct indicator of glycemic control or metabolic derangement in patients with T2DM. Additionally, we investigate correlation between FBG and HbA1c in T2DM patients and analyze association between SUA levels and glycemic parameters.

MATERIAL & METHODS

Source of Data and Study Design: This was a hospital-based cross-sectional observational study conducted in the Department of Biochemistry in collaboration with the Department of Medicine at Dr. S.N. Medical College in Jodhpur, (Rajasthan). Samples were analyzed for biochemical investigations in the Department of Biochemistry, Dr. S.N. Medical College in Jodhpur, (Rajasthan).

Study Population: A total of 150 patients with clinically diagnosed Type 2 Diabetes Mellitus were enrolled. Patients were selected based on predefined inclusion and exclusion criteria.

Inclusion Criteria:

- Age between 30–70 years.
- Diagnosed cases of Type 2 Diabetes Mellitus as per American Diabetes Association (ADA) guidelines.
- Patients providing informed written consent.

Exclusion Criteria: Patients with Type 1 Diabetes Mellitus, Pregnant or lactating women, chronic kidney disease, gout, liver cirrhosis, or those on uric acid-lowering drugs, Alcoholics are excluded from the study.

Sample Collection: Venous blood samples (5 mL) were collected from patients after overnight fasting (8–10 hours). Samples were processed for:

- **Fasting Blood Glucose (FBG):** Measured by glucose oxidase-peroxidase (GOD-POD) method.
- **Glycated Hemoglobin (HbA1c):** Measured using ion-exchange high-performance liquid chromatography (HPLC).
- **Serum Uric Acid (SUA):** Estimated using the uricase-peroxidase method.

All estimations were carried out using automated clinical chemistry analyzers as per the standard operating procedures in NABL-accredited laboratories.

Statistical Analysis: Data were analyzed using SPSS version. Mean and Standard Deviation were used to determine the data. Pearson correlation coefficient (r) was used to evaluate the

relationships between serum uric acid and glycemic markers. A p-value less than 0.05 were considered statistically significant.

RESULTS

The study included 150 patients of T2DM of age group of 30 to 75 years. There are 84 (56%) and 66 (44%) were males and females patients. Patients having HbA1c > 8% significantly higher SUA levels compared to those with controlled glycemia (HbA1c ≤ 7%).

Table No 1: Shows Descriptive Statistics of Parameters in Type 2 DM Patients.

Parameters	Mean ± SD
Age (years)	52.4 ± 10.7
Fasting Blood Glucose (mg/dL)	164.3 ± 42.5
HbA1c (%)	8.3 ± 1.6
Serum Uric Acid (mg/dL)	6.2 ± 1.4

Table No 2: Shows Correlation Analysis of Variables in Type 2 DM Patients.

Variables	Pearson's Correlation (r)	p-value
Fasting blood glucose vs HbA1c	0.78	0.001
Serum Uric Acid vs HbA1c	0.36	0.002
Serum Uric Acid vs Fasting blood glucose	0.29	0.015

Not significant ($p > 0.05$) and **Highly significant** ($p < 0.001$)

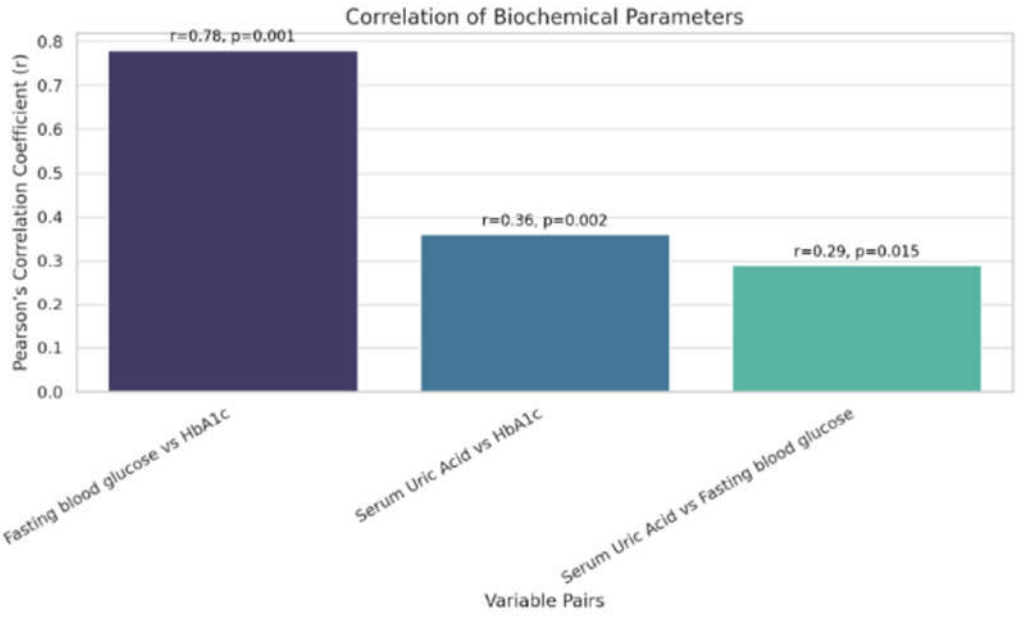

Figure No 1: Shows Correlation Analysis of Variables in Type 2 DM Patients.

DISCUSSION

A multifactorial metabolic disorder, T2DM, is predominantly characterized by chronic hyperglycemia that ensues from insulin resistance and relative insulin deficiency. Global escalation of T2DM prevalence has prompted extensive research into not only glucose metabolism but also the broader biochemical and physiological disturbances that accompany the disease. Purpose of this investigation was to examine interrelationship between SUA, HbA1c, and FBG levels in patients suffering from T2DM, thereby providing insight into whether SUA capable of serving as ancillary marker of glycemic control.

The utility of FBG and HbA1c in diabetes management is well established. FBG provides a snapshot of the patient's glucose levels at a single time point, reflecting short-term glycemic status, while HbA1c offers a more comprehensive view of the average blood glucose concentrations over the preceding 8–12 weeks. The significant positive correlation observed in this study between FBG and HbA1c ($r=0.78$, $p<0.001$) reaffirms reliability of these markers in glycemic monitoring.

For instance, Ketema EB et al. (2015) revealed that postprandial plasma glucose (PPG) has a closer association with HbA1c than fasting blood glucose (FBG). Therefore, in the absence of HbA1c, PPG is more accurate in forecasting total glycemic control.[10] Baishya R et al. (2023)

revealed that HbA1C levels exhibit a significant linear positive correlation with fasting and postprandial blood glucose levels. [11]

Recent evidence has positioned SUA as potential biomarker of systemic metabolic dysfunction, including its emerging role in T2DM. In our study, SUA levels have risen in a significant proportion of T2DM patients, especially those with poor glycemic control (HbA1c>8%). Moreover, SUA exhibited a moderate positive correlation with HbA1c ($r=0.36$, $p=0.002$) and statistically significant yet weakened correlation with FBG ($r=0.29$, $p=0.015$).

For an extended period, elevated SUA levels had been linked to other metabolic disorders, like dyslipidemia, hypertension, and obesity—all of which is commonly seen in diabetic patients. Clinical and experimental studies have corroborated correlation between hyperuricemia and insulin resistance, suggesting that SUA may not just be a byproduct of metabolic dysfunction but also a potential contributor to disease progression.

These findings are consistent with prior reports suggesting that hyperuricemia may be a surrogate indicator of insulin resistance and metabolic stress. Insulin resistance in T2DM may decrease renal excretion of uric acid, resulting in elevated serum levels. Secondly, hyperglycemia and oxidative stress up regulate xanthine oxidase activity, increasing uric acid production.

Our results correspond to those of Bhole et al. (2010), who reported a significant association between hyperuricemia and the incidence of metabolic syndrome and T2DM. [12] Similarly, Kodama et al. (2009) conducted a meta-analysis confirming a positive correlation between SUA levels and insulin resistance markers. [13] Research by Dehghan et al. (2008) also suggested that SUA is predictor of incident diabetes, independent of other metabolic risk factors. [14] However, contrary findings have also been reported. Choi et al. (2008) noted an inverse relationship between SUA and glycemic control in individuals with longstanding diabetes, potentially attributable to diabetic nephropathy impairing uric acid handling. [15]

One of the ongoing debates in medical literature revolves around whether SUA is merely a marker of metabolic derangement or a direct contributor to disease progression. Experimental studies have shown that endothelial dysfunction is induced by uric acid through inhibition of

nitric oxide bioavailability, thereby impairing insulin signaling and vasodilation. It also promotes vascular smooth muscle proliferation, contributing to atherosclerosis. These mechanisms provide biological plausibility that elevated SUA may not only reflect but also amplify the metabolic disturbances in T2DM. [16]

Results of current research affirm the hypothesis that SUA might function as adjunctive marker in assessing metabolic status in T2DM. Given that uric acid testing is inexpensive, widely available, and routinely performed in clinical settings, incorporating it into diabetes workups could enhance risk stratification. For instance, diabetic patients with hyperuricemia may warrant more aggressive management strategies to prevent complications, particularly cardiovascular and renal sequelae.

The limitations of the present study include design limitations in establishing temporal or causal relationships between SUA and glycemic markers. The findings may not be generalizable to the wider population due to the single-center, hospital-based nature of the study. Factors such as dietary purine intake, renal function (e.g., eGFR), use of medications affecting uric acid, and duration of diabetes were not fully controlled. A longitudinal study would better assess whether changes in serum uric acid parallel glycemic progression or regression.

CONCLUSION

This study investigated the interrelationship between FBG, HbA1c, and SUA levels within patients having T2DM. Our results demonstrated a strong positive correlation between FBG & HbA1c, which is expected given their shared role in reflecting glycemic status. We observed that SUA levels had statistically significant positive correlation with both FBG and HbA1c, albeit to a lesser extent. Present outcomes suggest that higher SUA levels are associated with poorer glycemic control within patients having T2DM.

Conflicts of Interest: None

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