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Original Research Paper

Biochemistry

# EFFECT OF SERUM GAMMAGLUTAMYL TRANSFERASE AND URIC ACID ON INCIDENCE OF DIABETES MELLITUS

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## ABSTRACT

**Introduction :**The incidence of diabetes mellitus is increasing among the Asian populations as well as in the Western countries. People with diabetes are at elevated risk for a number of serious health problems .Diabetes is often asymptomatic in its early stages and can remain undetected for several years. Therefore, early diagnosis of the condition is important as careful diabetes management can reduce long-term complications. According to recent studies, serum gamma -glutamyl transferase (GGT) and serum uric acid (UA) are emerging potential markers of diabetes development.

Objective of study The aim of this study was to explore the relationship between GGT, UA and diabetes.

**Materials And Methods:** This study is conducted in Biochemistry department of Dr BSA Medical College & Hospital, Delhi .All the fasting serum samples coming to the OPD between November to December 2019, fulfilling the inclusive criteria (i.e. patients aged between 40-70 years) are included in the study. The total number of subject fulfilling the criteria was found to be 264. 3ml of venous blood has been collected under all aseptic precaution and used for estimation of oxidative stress markers like gamma glutamyl transferase and serum uric acid.

Normality of the data has been checked by Kolmogorov -smirnov test. Mann-Whitney U test has been applied to check whether the distribution of YGT and Uric Acid is same across categories of level of Blood sugar. Spearman's correlation coefficient has been calculated instead of Pearson correlation between Fasting Blood Sugar, Uric acid and YGT. All Statistical analysis has been performed with SPSS 22.0, p value of $\leq 0.05$ has been considered to be statistically significant.

**Results:** Among all the eligible subjects included in the study, the mean ± S.D. of different study variables are; fasting blood sugar (160.80±87.44), Uric Acid (5.47±1.74) and YGT(49.50±111.77). All the three variables are found to be Non-normal. YGT is found to be significantly positively correlated with Fasting BS (r=0.222,p-value=0.000) and Uric acid (r=0.235,p-value=0.000). We found that the distribution of YGT is significantly differ among the categories of Blood sugar level (p-value=0.006). However from the data we do not found significant difference of Uric acid across the categories of Blood sugar level(p-value=0.723).we observed that serum GGT and UA levels increased in diabetes patients whose fasting FPG is >126mg/dl .

**Conclusion:** Higher serum GGT and UA levels were found to be associated with greater risk of diabetes, suggesting that they may serve as valuable clinical markers for the future development of diabetes. Thus estimation of the above said parameters regularly will help in the better management of the diabetes patients and proves as better prognostic markers in such patients.

## KEYWORDS :

## INTRODUCTION

The incidence of diabetes mellitus is increasing among the Asian populations as well as in the Western countries.[1] People with diabetes are at elevated risk for a number of serious health problems, including cardiovascular disease, premature death, blindness, kidney failure, amputations, and cognitive decline.[2]

Diabetes is often asymptomatic in its early stages and can remain undetected for several years.[3] Therefore, early diagnosis of the condition is important as careful diabetes management can reduce long-term complications.[4] According to recent studies, serum gamma-glutamyltran sferase (GGT) and serum uric acid (UA) are emerging potential markers of diabetes development.[5–9].

Serum GGT is an enzyme that has a pivotal role in the maintenance of intracellular antioxidant defenses,[6] and some studies have suggested that oxidative stress could be involved in the development of diabetes.[7,8] Also,mounting evidence indicates that GGT relates to incidence of prediabetes and diabetes in adults, and is an appealing biochemical risk indicator for diabetes prediction.[10–12]In addition, serum UA, a by-product of oxidation of purines that is filtered by glomeruli in the kidney and reabsorbed by the proximal tubule, may promote insulin resistance by inhibiting endothelial cell function.[9,13] Indeed, some studies found that higher serum UA is associated with higher future risk of diabetes, independent of other known risk factors.[5,14]

## AIM OF STUDY

The aim of this study was to investigate the combined association of increased serum GGT and serum uric acid levels in development of type 2 diabetes.

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### Inclusion Criteria:

1.Patients aged between 40-70 years of either sex

### 2.Exclusion Criteria:

Critical ill patients

- Patients aged either <18 years and >60 years of either sex.
- Female patients with menstruation/pregnancy

## METHODOLOGY

1. Three millilitre of venous blood will be collected under all aseptic precaution and used for estimation of oxidative stress markers like gamma glutamyl transferase and serum uric acid.

The patients will be divided into 2 groups according to their fasting blood glucose level: >126mg/dl and <126mg/dl Glucose is estimated by GOD-PAP method by mindry BS 480 autoanalyser.

Uric acid is estimated by using uricase method by mindry BS480 autoanalyser.

GGT is estimated by szasz methodology by mindry BS 480 autoanalyser

## RESULTS

### Statistical Analysis

Statistical analysis has been performed with SPSS 22.0 (SPSS Inc. Chicago, USA).The continuous variables has been presented as mean ± standard deviation. Normality of the data has been checked by Kolmogorov-smirnov test. Mann-Whitney U test has been applied to check whether the distribution of YGT and Uric Acid is same across categories of level of Blood sugar. Since the data is non-normal, Spearman's correlation coefficient has been calculated instead of Pearson correlation between Fasting Blood Sugar, Uric acid and YGT.

A p value of ≤0.05 will be considered to be statistically significant.

## RESULTS:

Among all the eligible subjects included in the study, the mean ± S.D. of different study variables are; fasting blood sugar (160.80±87.44), Uric Acid(5.47±1.74) and YGT (49.50±111.77). All the three variables are tested for normality by using Kolmogorov-Smirnov test, where we found that fasting blood sugar, Uric Acid and YGT all are non-normal. (See table 1)

**Table 1: Basic Descriptive Of Variable**

| Variable | Mean | Std. Deviation | p-value* |
|---|---|---|---|
| Fasting BS | 160.8070 | 87.44657 | 0.000 |
| Uric Acid | 5.478409 | 1.7395281 | 0.000 |
| YGT | 49.500000 | 111.7767799 | 0.000 |

*Kolmogorov-Smirnov test is applied to check the normality.

**Table 2: Correlation between the Fasting BS, Uric Acid and YGT**

| | | | Fasting BS | Uric Acid | YGT |
|---|---|---|---|---|---|
| Spearman's rho | Fasting BS | Correlation Coefficient | 1.000 | -.063 | .222** |
| | | Sig. (2-tailed) | . | .304 | .000 |
| | Uric Acid | Correlation Coefficient | -.063 | 1.000 | .235** |
| | | Sig. (2-tailed) | .304 | . | .000 |
| | YGT | Correlation Coefficient | .222** | .235** | 1.000 |
| | | Sig. (2-tailed) | .000 | .000 | . |

**. Correlation is significant at the 0.01 level (2-tailed).

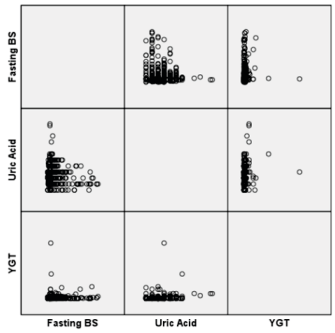


**Figure 1: Correlation Matrix Plot Of Fasting Bs, Uric Acid And Ygt**

From Table 2 and Figure 1, we see that YGT is significantly positively correlated with Fasting BS (r=0.222,p-value=0.000) and Uric acid (r=0.235,p-value=0.000). However the correlation is not so strong but it shows significant positive correlation.

Independent samples Mann-Whitney U Test has been applied to check whether the distribution of YGT is same across the categories of Blood Sugar level. Here we found that the distribution of YGT is significantly differ among the categories of Blood sugar level (p-value= 0.006). However from the data we do not found significant difference of Uric acid across the categories of Blood sugar level(p-value=0.723).

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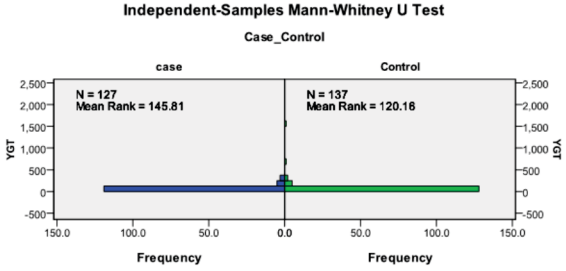


| | |
|---|---|
| Total N | 264 |
| Mann-Whitney U | 10,390.000 |
| Wilcoxon W | 18,518.000 |
| Test Statistic | 10,390.000 |
| Standard Error | 619.582 |
| Standardized Test Statistic | 2.728 |
| Asymptotic Sig. (2-sided test) | .006 |

## DISCUSSION

In the present study, we compared the blood biochemical parameters between the patients will be divided into 2 groups according to their fasting blood glucose level: >126mg/dl and <126mg/dl in a population derived from a crosssectional observational survey,where we received the samples from routine OPD Dr BSA medical college . we observed that serum GGT and UA levels increased in diabetes patients whose fasting FPG is >126mg/dl . The present study also evaluated whether there was a synergistic effect between serum GGT and UA on the development of diabetes .GGT and UA were significantly higher compared with the reference group. This finding may be supported by the observation that both GGT and UA were associated with oxidative stress and inflammation.[16,17] In the present study, we found an significantly raised gamma glutamyltransferase levels in diabetic patients group than compared to control groups, which is evident and consistent from other recent studies[18]. GGT protein catalyzes an enzymatic action, which is the transfer of a glutamyl residue to an acceptor through the glutamate's gamma carboxylic acid to an amine or other amino acid. The most abundant natural substrate is glutathione. Glutathione is extracellular and cannot pass through the cell membrane. Adequate supply of intracellular glutathione protects cells against oxidants produced by normal metabolism[19]. Glutathione can be broken down into 3 amino acids (including cysteine, which may be deficient in

low-protein diets) at the cell membrane by GGT. Figure 1 shows suspected pathways relating GGT to type 2 diabetes . It is likely that insulin resistance leads to increased fat deposits in the liver, which cause oxidative stress and inflammation, leading to type 2 diabetes[20]. Increased GGT activity can be a response to oxidative stress,indicative of marked transportation of glutathione into cells. In this regard, increased serum GGT may identify those individuals with persistently higher oxidative and other cellular stress levels. Pancreatic beta-cells are particularly vulnerable to oxidative stress as they have relatively low levels of reactive oxygen intermediate scavenging enzymes such as superoxide dismutase, catalase, and glutathione peroxidase.[21] Indeed, oxidative stress is known to impair insulin secretion by pancreatic beta-cells.[22] UA is an end product of purine metabolism and is related to the purine bases of the nucleic acids in humans. The serum UA level is determined by the balance between purine intake and UA production. Approximately two thirds of total body urate is produced endogenously, the remaining one third is accounted for by dietary purines. Approximately 70% of the urate produced daily, however, is excreted by the kidneys. The rest is eliminated by the intestines. Long-term hyperuricemia is a causal factor to damage development in the joints, connective tissues, and kidney. Hyperuricemia and may predispose to, hypertension, diabetes . The relationship between UA and diabetes may involve deposition of UA in islets, which could lead to β cell damage and functional decline, resulting in impaired glucose handling. The pro-inflammatory and oxidative stress effects of UA may also be possible causes of impaired glucose handling [23]. Several studies have suggested that UA may promote insulin resistance by leading endothelial dysfunction and nitric oxide inhibition.[23] In addition, UA can also cause oxidative damage of pancreatic beta cells.[24,25] These mechanisms may be responsible for the association of GGT and UA levels with the onset of diabetes.

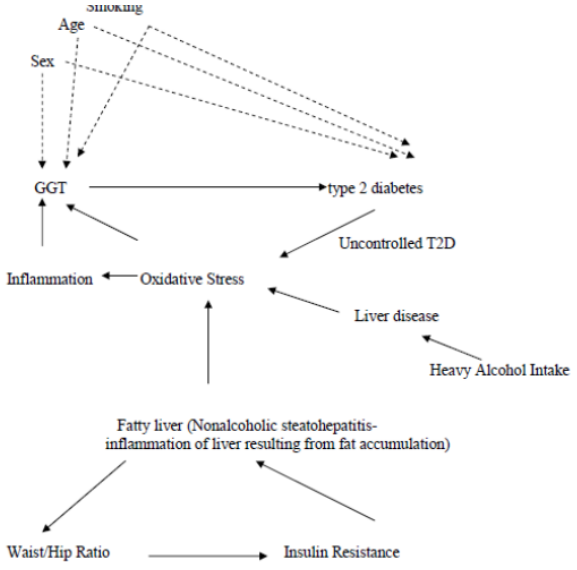


*Figure 1.* Diagram of known and theoretical pathways.

## CONCLUSION

We found that higher serum GGT and UA levels were associated with greater risk of diabetes, suggesting that they may serve as valuable clinical markers for the future development of diabetes. Thus estimation of the above said parameters regularly will help in the better management of the diabetes patients and proves as better prognostic markers in such patients Further studies are needed to elucidate the temporal nature of these associations, and to determine the reason why high serum GGT and UA levels are at greater risk of diabetes .

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