Gamma glutamyl transferase in Type II diabetes mellitus patients attending tertiary care academic hospital

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ABSTRACT

Background: Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. It is a leading cause of mortality and morbidity in adults worldwide, posing serious medical, socioeconomic, and rehabilitation problems. Rapid diagnosis plays an important role in the management of DM. Gama glutamyl transferase (GGT) is an example of one of these biomarkers. **Aims and Objectives:** The aim of the study was to study the correlation of GGT in Type 2 DM patients. **Materials and Methods:** The present cross-sectional study was carried out in the Department of Biochemistry, B.J. government Medical College and Sassoon General Hospital Pune, Maharashtra. The study period was from December 2015 to June 2017. A total of 70 newly diagnosed Type 2 DM patient aged between 40 and 60 years with blood glucose level more than 126 mg/dL in fasting and more than 200 mg/dL post-prandial were included in the study. **Results:** The mean GGT in control group was 26.5 U/L and in diabetic group was 58.5 U/L. The GGT values were significantly raised in diabetic (case group) as compared to control group (P < 0.0017). **Conclusion:** GGT can be considered as an important biomarker in monitoring and preventing complication associated with Type 2 DM.

Key words: Diabetes mellitus; Biomarker; Gama glutamyl transferase

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin.[1] The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health-care system.[1]

The worldwide prevalence of DM has risen dramatically over the past two decades from an estimated 30 million cases in 1985 to 2463 million in 2019. Based on the current trends, the International Diabetes Federation projects that 642,000,000 individuals will have diabetes by the year 2040.[2]

India is home to 77 million diabetics, second only to China in the world. The Government of India and Diabetic Retinopathy Survey 2019 found 11.8% prevalence of diabetes in India. The prevalence was higher in urban areas ranging between 10.9% and 14.2%.[2]

Although the prevalence of both Type 1 and Type 2 DM is increasing worldwide, the prevalence of Type 2 DM is rising much more rapidly.

Early diagnosis of the complications plays an important role in overall management of DM. As Type 2 DM is associated with chronic low-grade inflammation, several biomarkers related to inflammation can be applied for its diagnosis, assessment of treatment, and prognosis.[3] Gama glutamyl transferase (GGT) is an example of one

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of these biomarkers. GGT is present in decreasing order of abundance in proximal renal tubule, liver, pancreas, and intestine.[4]

GGT, E.C.2.3.2.2 is a cell-surface protein, contributing to the extracellular catabolism of glutathione (GSH). The enzyme is produced in many tissues, but most GGT in serum is derived from the liver. GGT has a pivotal role in the maintenance of intracellular antioxidant defenses through its mediation of extracellular GSH transport into most types of cells. Oxidative stress is associated with a number of pathological conditions, such as inflammation, carcinogenesis, aging, atherosclerosis, and reperfusion injury. Oxidative stress can also play a role in the cause and pathophysiology of diabetes.[5]

Low-grade inflammation is found in a number of pathological conditions such as aging, obesity, physical inactivity, atherosclerosis, hypertension, dyslipidemia, and hyperinsulinemia by mediating or inducing oxidative stress.[4] It implies that increased GGT concentration is associated with metabolic syndrome.

The serum concentration of GGT was more in impaired glucose tolerance (IGT) group, when compared to Type 2 DM, but statistically not significant, whereas when compared to controls, GGT was found raised significantly in both Type 2 DM and IGT.[6]

Aims and objectives
Correlation of Gamma glutamyl transferase (GGT) in type 2 Diabetes Mellitus patients.

MATERIALS AND METHODS

The present cross-sectional study was carried out in the Department of Biochemistry, B.J. government Medical College and Sassoon General Hospital Pune, Maharashtra. The study period was from December 2015 to June 2017.

A total of 70 newly diagnosed Type 2 DM patient aged between 40 and 60 years with blood glucose level more than 126 mg/dL in fasting and more than 200 mg/dL post-prandial were included in the study.

A signed informed consent was obtained as per the proforma from all the subjects or their legally responsible attendants. The protocol of the study was approved by the institutional ethical committee.

The following were the exclusion criteria:
1. Patients with recent clinical infection, chronic inflammatory condition or neoplastic diseases
2. Bleeding disorders, cerebral hemorrhage of any etiology, and autoimmune disorders
3. Conditions mimicking stroke (metabolic problems such as hepatic encephalopathy, CNS problems such as hemiplegic migraine, subdural hematoma, and abscess)
4. Patients with history of surgery or major trauma in the previous month
5. Patients with any major renal, hepatic disease, alcoholic liver disease, or chronic alcoholism
6. Ongoing cardiac ischemia and known peripheral vascular disease.

In addition, a total of 70 age- and sex-matched healthy individuals without any major illness and not on any medication willing to give their consent were included as controls. About 2ml of blood samples were obtained from the antecubital vein of each subject and control. The blood samples were transferred to clean dry sterile plain vacutainers and allowed to clot for 30 min and then centrifuge.

The serum samples were used for estimation of gamma GT levels. GGT transfers the ϒ-glutamyl-3-caboxy-4-nitroanilide to glycylglycine. The amount of 5-amino-2-nitrobenzoate liberated is proportional to the GGT activity and can be determined photometrically.

RESULTS

As shown in Table 1, the mean age of distribution of cases and controls were 50 ± 6.2 and 50 ± 5.8 years, respectively. There was no significant difference observed between age distributions among the two groups (Mann–Whitney test P>0.05). In Group 1 (controls) out of 70, 43 (61.4%) were males and 27 (38.6%) were female participants, whereas in Group 2 (cases) out of 70 Type2 DM patients, 45 (64.2%) were males and 25, (35.8%) were females. There was no significant difference between gender distributions among the two groups (Mann–Whitney test P>0.05).

The serum GGT level and its comparison among a study group is shown in the Table 2. The mean GGT in control group was 26.5 mg/dL and in diabetic group was 58.5 mg/dL. The GGT values were significantly raised in the diabetes cases as compared to the control group.

The GGT values were significantly raised in Diabetic (case group) as compared to control group (P<0.0017) as shown in Table 3.

Chart 1 given below comparing GGT in control and cases.

Table 4 shows P=0.0017 which is in accordance with Wang and Koh study 2017.
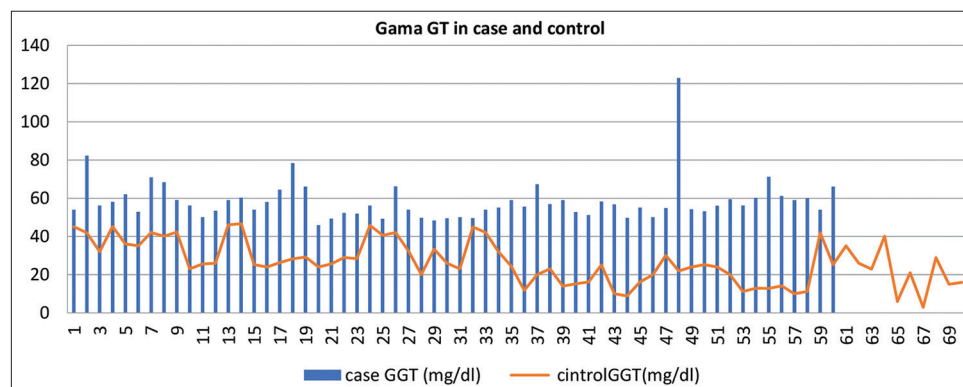
Chart 1: Compairing gama glutamyl transferase in control and cases

Table 1: Age distribution of case and control

Statistical data	Control	Cases
Mean±SD	50±5.8	50±6.2
Median	49	50
Minimum	40	40
Maximum	60	60

Table 2: Comparison of gamma glutamyl transferase

Parameter	Mean±SD	
	Control	Cases
Gama GT (mg/L)	26.5±11.2	58.5±10.5

Table 3: P value (Significance) of gamma glutamyl transferase

Parameter	P-value (level of significance-t test)
	Control versus Cases
Gama GT	0.0017(HS)

Table 4: Tabular results of GGT with random blood glucose

Testing sensors	GGT (U/l)
No. of XY pairs	70
Pearson r	0.3677
95% confidence interval	0.1452–0.5548
P-value (two-tailed)	0.0017
P-value summary	**
Is the correlation significant? (alpha=0.05)	Yes
R squared	0.1352

DISCUSSION

The burden of diabetes is high and increasing globally, and in developing economies like India, it is mainly being fuelled by the increasing prevalence of overweight, obesity, and unhealthy lifestyles. The estimates in 2019 showed approx. 77 million individuals with diabetes in India, which is expected to rise to over 134 million by 2045. Type 2

diabetes, which accounts for majority of the cases, can lead to multiorgan complications, broadly divided into microvascular and macrovascular complications.[7]

In this study, a total of 70 diabetic patients attending outpatient service of Department of Medicine were studied and matched with 70 healthy controls with respect to their age and gender. The age distribution of the patient in this study was between 40 and 60 years. Average mean age was 50.8 years in case group and 50.08 years in control group. The risk of Type 2 DM was found increasing with the increasing age.[4]

Insulin resistance and abnormal insulin secretion are central to the development of Type 2 DM. Although the primary defect is controversial, most studies support the view that insulin resistance precedes an insulin secretory defect, but that diabetes develops only when insulin secretion becomes inadequate. Type 2 DM likely encompasses a range of disorders with a common phenotype of hyperglycaemia.[2]

Serum GGT was also correlated with insulin resistance-markers, waist-circumference, triglycerides, fasting plasma glucose, HbA1c, systolic, and diastolic blood pressure.[8]

Although the biological mechanisms are not completely understood, mounting evidence suggests that GGT and UA may be involved in the development of diabetes. Concerning GGT levels, serum GGT may predict diabetes incidence as a marker for oxidative stress related to GSH levels, with GSH performing critical antioxidant defense for the cell. Increased GGT activity can be a response to oxidative stress and indicative of marked transportation of GSH into cells. In this regard, increased serum GGT may identify the individuals with persistently higher oxidative and other cellular stress levels. Pancreatic β-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 GSH peroxidase. Indeed, oxidative stress is known to impair insulin secretion by pancreatic β-cells.[9]

In our study, the Gama GT levels in Type 2 DM patients were estimated and compared with those of healthy controls. It was found that the levels in Type 2 DM patients were 58.5 mg/dL, whereas in control group were 26.5 mg/dL. The GGT values were significantly raised in diabetic case group as compared to control group with $P<0.0017$. A similar observation was noted by Wang and Koh Study in 2017. GGT was assayed among 255 type 2 DM cases with baseline hemoglobin A1c <6.5% and same number of matched controls. Higher levels of ALT and GGT were significantly associated with increased risk of type 2 DM.[10]

Limitations of the study

The limitation of the present study was the small sample size. Furthermore, patients with mild liver disease were not excluded from the study.

CONCLUSION

The findings of the study can have practical and clinical implications in the early diagnosis of Type 2 DM. Despite of the limitation measurement of gamma GT in this population, it may be considered as an important biomarker in monitoring and preventing the complication associated with Type 2 DM.

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Author's Contributions:
RS- Concept and design of the study; prepared first draft of manuscript; interpreted the results, reviewed the literature, and manuscript preparation; **SR-** Coordination and statistical analysis; **R-** Data interpretation and statistical analysis; **C-** Revision of the manuscript. **N-** Revision of the manuscript

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