International Journal of Clinical Biochemistry and Research 2019;6(3):336–339

Content available at: iponlinejournal.com

International Journal of Clinical Biochemistry and Research

Journal homepage: www.innovativepublication.com

Original Research Article

Analysis of serum gamma glutamyl transpeptidase (GGT) level as a marker for the detection of type 2 diabetes mellitus in Okhla industrial area

Juhi Aggarwal[1],*, Niharika Singh[2], Mayur Kumar[3]

[1]*Dept. of Biochemistry, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh, India*
[2]*Dept. of Biochemistry, Mayo Institute of Medical Sciences, Barabanki, Uttar Pradesh, India*
[3]*Esic Hospital, Delhi, India*

ARTICLE INFO

Article history:
Received 03-06-2019
Accepted 08-07-2019
Available online 21-09-2019

Keywords:
Diabetes mellitus type 2
Gamma Glutamyl Transpeptidase
Glycosylated hemoglobin
Oxidative stress
MDA

ABSTRACT

Introduction: Diabetes Mellitus is one of the world's leading non communicable public-health problems. It is a endocrine disorder resulting either from absolute deficiency of insulin or their is resistance to insulin action. γ- Glutamyl Transpeptidase (GGT) might reflect metabolic disorder and could serve as a marker for insulin resistance. Raised serum GGT activity which is observed in these diabetic patients is in response to increased apoptosis and oxidative stress that occurs during the course of the disease. Thus, this study was performed to examine γ- Glutamyl Transpeptidase as a useful bio marker for the detection of type 2 diabetes mellitus.

Materials and Methods: A total of 250 individuals were selected from the OPD, medicine department at ESIC hospital, Okhla and 250 normal healthy adults were selected as controls. The data was collected from a period of over 8 months i.e. March 2018 till October 2018.

Result: The study showed higher levels of glycosylated hemoglobin (HbA1c), GGT and malondialdehyde (MDA) levels in the study group when compared to control group. The increased levels of GGT are associated with insulin resistance, oxidative stress and also involved in the development of type 2 diabetes mellitus.

Conclusion: Study suggested the levels of Fasting Blood Sugar, Post Prandial Blood Sugar, HbA1c, MDA and GGT increased in the DM type 2 patients as compared with that of normal persons. Hence, GGT which is a marker of Oxidative stress was also raised in cases of DM type2.

1. Introduction

Diabetes is a common clinical condition affecting above 10% of the general population (more prevalent after the age of 50 years) but nowadays it is becoming prevalent among age groups between 30 to 45 years also. Change of lifestyle, increased calorie intake, environmental factor, junk food, sedentary life and stressful life are among the causes for such a spurt in diabetes in India. It is a metabolic disorder resulting either from deficiency of insulin or resistance to its action causing increased blood glucose level (hyperglycemia) which leads to several systemic complications. In humans, diabetes occurs due to destruction of β cells of pancreas or due to decreased sensitivity of insulin receptors to insulin. Insulin resistance is defined as a decreased biological response to normal levels of circulating insulin. [1]

Diabetes mellitus is characterized by polyuria, polyphagia, polydipsia, weight loss in spite of increased food intake, hyperglycemia and glycosuria. Factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization and increased glucose production. Recently, the incidence of diabetes mellitus in India is rated highest amongst all the countries in the world. The burden of patients suffering from diabetes will double by 2025. There are almost one million casualties per annum in India. [2]

It usually affects the individual after 40 years of age (hence it is also called adult-onset diabetes). Diagnostic

* *Corresponding author*.
E-mail address: jaggarwal38@gmail.com (J. Aggarwal).

https://doi.org/10.18231/j.ijcbr.2019.073
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criteria by the American Diabetes Association (ADA) include the following:[3]

1. A fasting plasma glucose (FPG) level of ≥ 126 mg/dl.
2. A post prandial plasma glucose level (PPG) of ≥ 200 mg/ dL.
3. A random plasma glucose level of ≥200 mg/dl.
4. Glycosylated Hemoglobin (HbA1c) level of ≥6.5%.

Gamma-glutamyl cycle is a cyclical process which involves the synthesis and degradation of glutathione. The enzyme gamma-glutamyl transpeptidase releases glutamate from glutathione.[4] Thus, GGT plays a central role in regulation of glutathione homeostasis. Glutathione is most useful in maintaining the overall redox functions and in detoxification of electrofiles.[5,6]

Serum GGT serves as a clinical marker of overall hyperinsulinaemia, hepatic and systemic insulin resistance.[7] GGT can serve as an independent risk predictor of type-2 diabetes mellitus because of its strong association with insulin resistance and also independent with respect to other confounding factors like age, alcohol intake, physical activity, positive family history of diabetes mellitus, fatty liver, smoking habits and hypertension.[8] Serum GGT is also known as a marker of alcohol-induced liver disease.[9] GGT reflects metabolic derangements and could serve as a indicator for insulin resistance and metabolic syndrome.[10] Emerging evidence suggests that elevated GGT levels show disturbances in the glucose and lipid metabolism and can act as a predictor of liver disease and cardio vascular damage.[11]

Thus, the present study was conducted to investigate the serum GGT levels as the marker to detect the patients of type 2 diabetes mellitus in both males and females in our study population.

2. Materials and Methods

This study was conducted on the diabetic patients with the age group of 45-65 years in the Department of Biochemistry, ESIC Hospital, Okhla. It comprised of total of 500 individuals and the study period was from March 2018 to October 2018. Out of which each group included 250 adult individuals suffering from type 2 diabetes mellitus & normal healthy adults as controls respectively. The subjects with any acute and chronic disease, severely anaemic (<6.0gm% of Hb) and those suffering from any other systemic disorder were excluded from the study. Well informed written consent was obtained from all the enrolled subjects. Institutional ethical committee was also taken into the account. A detailed clinical history including age, sex, occupation, socio-economic status, duration of diabetes and any associated risk factor contributing for the illness was elicited from the subjects. With all aseptic precautions, blood samples (5 ml) were drawn by venipuncture and collected in plain and EDTA tubes to measure Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), MDA (malondialdehyde), HbA1c and GGT levels. They were measured using an enzymatic colorimetric method (Modular P; Roche Diagnostics).

The method of thiobarbituric acid, which measured MDA-reactive products i.e. thiobarbituric acid reactive substance (TBARS), there was formation of pink colour and was read at 532 nm using spectrometer.[12]

2.1. Statistical analysis

The result are presented in mean ± SD. FBS, PPBS, MDA, and GGT levels were compared by using Unpaired t-test between cases and controls. The Pearson's correlation coefficient were calculated among the study parameters. The p- value <0.05 was considered significant. All the analysis was carried out by using SPSS version.

3. Observations

P-Probability

The levels of cases is higher as compared to controls and the difference was statistically significant.

4. Result

1. The level of FBS was observed to be higher among cases 128.0 ± 13.4 compared with control 100.4 ± 9.6.
2. The level of PPBS and HBA1c was increases in cases 254.3 ± 59.0, 8.49± 1.05 compared with control 118.6 ± 34.6, 5.36 ± 1.2.
3. The level of MDA is also higher in cases 3.62 ± 1.20 compared with control 0.89 ± 0.46.
4. The values of FBS, PPBS, HBA1c and MDA were found to be significantly increased with p- value < 0.001.

5. Discussion

A total of 250 normal and same number of individuals having diabetes mellitus were recruited for the study in ESIC hospital, Okhla. Studies suggested that the serum GGT is ubiquitously present in all the cells. Though its primarily related to the liver pathology its also indicated in cardio vascular disease, alcohol consumption and metabolic syndrome.

In a data collected from the DESIR cohort in 2007, it was found that as compared to women, men had higher concentration of GGT. GGT was significantly associated with the course of study period in relation to BMI, levels of serum triglyceride and insulin, blood pressure measurement.[13]

In a cross-sectional study done by Sabanayagam C et al in US adults aged ≥ or = 20 years, involving 7,976 participants it was showed that serum GGT levels were significantly associated with diabetes mellitus.[14] In a 4 year follow-up study for the men working in a steel

Table 1: Demography profile of cases and controls

S. No	Parameters	Control	Cases
1	Number of cases	250	250
a	Males	140	134
b	Females	110	116
2	Mean/average age (years)	48.2 ± 10.3	51.3 ± 8.4

Table 2: Comparison of biochemical parameters between cases and controls

S.No	parameters	control	cases	p- value
1	FBS (mg/dl)	100.4 ± 9.6	128.0 ± 13.4	< 0.001
2	PPBS (mg/dl)	118.6 ±34.6	254.3 ±59.0	< 0.001
3	HbA1c (%)	5.36± 1.2	8.49± 1.05	< 0.001
4	MDA (μ mol/L)	0.89± 0.46	3.62± 1.20	< 0.001

manufacturing company, by Lee DH et al, it was suggested that an increase in GGT concentration is a highly sensitive biomarker for the development of diabetes.[15]

It was assessed in a study done by Kim CH et al in 2,024 non-diabetic subjects with non alcoholic fatty liver disease (NAFLD) it was observed that SGPT was significantly related with the hepatic fat accumulation than GGT. Since, GGT is involved in the redox maintainence in our body increased GGT activity can be associated with increased oxidative stress and insulin resistance.[16] In a 2005 report, performed by researchers in North Western Italy in 45-64 age population, it was evident that those with the highest GGT levels present with higher fasting glucose, hs-CRP and nitrotyrosine values in male subjects and is an early marker of cellular stress.[17]

In a study of total 172 cases suffering from diabetes mellitus it was depicted that females obesity was directly proportional to the higher GGT values. However, in males this association was not seen.[18]

In a cohort study conducted in Finland in middle-aged men and women, independent of alcohol intake the inter-relationship with BMI and serum GGT levels was described. It was found that in both men and women with higher GGT levels there is a proposed risk of these subjects suffering from diabetes mellitus type 2.[19]

Haghighi S et al in 2011 selected the first-degree relatives (FDR) of pre-diabetes and type 2 diabetes patients. The researchers found that was a positive association in the GGT levels and the development of full blown diabetes disease which was confirmed by the glucose intolerance curve of the subjects. This trend was more visible in the male population as compared with the females.[20]

In an ethnic group based study of the adult U. S. nationals by Lim JS et al GGT was depicted as an early biomarker to indicate the oxidative stress. The anti oxidants like carotenoids, lycopene, and vitamin C were inversely related to the serum concentrations of GGT.[21]

6. Conclusion

The present study helped us to investigate diabetes mellitus type2 more precisely with GGT which further can be used for its early diagnosis and management. In this study, GGT was significantly associated with an increased risk of development of type 2 diabetes in adults particularly those with alcohol and smoking habits, obesity and sedentary lifestyle. The pathophysiology can be studied with increased ratio of metabolic syndrome, insulin resistance, oxidative stress, and chronic systemic inflammation. The elevated serum GGT concentrations may also help in identifying high risk people i.e. first degree relatives of the diabetics who would possibly benefit from lifestyle modification or earlier therapeutic interventions.

7. Source of support

None.

8. Conflict of interest

None.

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Author biography

Juhi Aggarwal Associate Professor

Niharika Singh Tutor

Mayur Kumar Specialist Grade II

Cite this article: Aggarwal J, Singh N, Kumar M. Analysis of serum gamma glutamyl transpeptidase (GGT) level as a marker for the detection of type 2 diabetes mellitus in Okhla industrial area. *Int J Clin Biochem Res* 2019;6(3):336-339.