*Original Article*

# Association of Serum Gamma Glutamyl Transferase Level with Impaired Fasting Glucose in Adults at a Tertiary Level Hospital of Bangladesh

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## Abstract

***Introduction***: Prediabetes is considered as significant risk factor of overt diabetes. Gamma glutamyl transferase is an oxidative stress marker that is synthesized in liver. Oxidative stress causes impaired insulin secretion from beta cells of pancreas. Serum Gamma glutamyl transferase level increases in persons with diabetes and cardiovascular disease.

***Objective:*** To find out the association of serum Gamma glutamyl transferase and impaired fasting glucose.

***Materials and Methods:*** This cross-sectional analytical study was carried out among 120 subjects aged 25–55 years in the Biochemistry department of Sir Salimullah Medical College, Dhaka during the period of March 2018 to February 2019. The subjects of the study were grouped as normal fasting glucose and impaired fasting glucose as per the criterion of WHO. Blood was collected to perform OGTT. Serum was separated to measure Gamma glutamyl transferase (GGT) and lipid profile.

***Results:*** GGT levels were significantly greater ($p$<0.01) in impaired fasting glucose (IFG) group than normal fasting glucose (NFG) group (67.2±14.4 vs 24.2±8.4). Odds Ratio (OR) for IFG were 4.1 and 20.3 with GGT tertile 2 (24.0-42.0) U/L and tertile 3 (>42.0) U/L where $T_1$ (< 24.0) U/L was considered as reference category. Multiple regression analysis was done to find out the relation between Fasting plasma glucose (FPG) and serum GGT by adjustment of other factors, which revealed that IFG was significantly ($p$< 0.01) associated with serum GGT.

***Conclusion:*** Subjects with IFG have higher serum GGT than NFG subjects and higher serum GGT level is associated with greater risk of IFG. Moreover, GGT has strong independent relationship with FPG. The association of serum GGT with IFG suggests that it can be used as adjuvant marker for risk assessment of DM and screening tool for economically underdeveloped country like Bangladesh.


***Key-words*:** Gamma glutamyl transferase, Prediabetes, Impaired fasting glucose.

## Introduction

Impaired fasting glucose is considered as one of the components of prediabetes. It is a contributing factor of diabetes and cardiovascular diseases[1]. Prediabetes is defined as impaired fasting glucose and /or impaired glucose tolerance[2]. Impaired fasting glucose is related to the development of insulin resistance. It is associated with a higher transformation from prediabetes to diabetes (approximately 25% in three years) in comparison to impaired glucose tolerance (IGT)[3]. In the United States (U.S.), nationwide surveys were conducted and found that among adolescents, prediabetes was prevalent[4]. A study conducted in China showed, prevalence of prediabetes was approximately 15.5%[5]. In the U.S. one of the important causes of death is impaired glucose homeostasis[6]. In developing countries, type 2 diabetes mellitus maybe raised to approximately 70% and in developed countries it will be increased by 20% in the year from 2010 to 2030 in adults[7]. So, early detection of this state is necessary as careful diabetes management can decrease long term complications[8].

Serum Gamma glutamyl transferase (GGT) and alanine aminotransferase are common indicators to hepatic disease. Recent studies showed that, Serum GGT and alanine aminotransferase concentration shows close association with prevalence of type 2 diabetes mellitus among certain populations[9]. Elevations of both the enzymes are related to metabolic syndrome. It is also related to the clinical presentations of type 2 diabetes mellitus (T2DM) and cardiovascular diseases[10].

The associations of plasma glucose level with serum GGT level were reported among Chinese adults[11]. Several studies carried out in the U.S. and different nations reported that GGT has a role to develop diabetes[12]. It was found that, hepatic enzymes associated with incident T2DM and metabolic syndrome are limited to middle and older populations[13]. However, there is limited published data regarding the association of serum GGT with impaired fasting glucose (IFG) in our country. So, it is very important to justify the validity of serum GGT as a biomarker to predict IFG in adults. Therefore, purpose of this study is to explore

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the association of serum GGT with IFG which will contribute to combat DM in Bangladesh.

## Materials and Methods

This cross sectional analytical study was conducted in the Biochemistry department of Sir Salimullah Medical College, Dhaka from March 2018 to February 2019. A total 120 subjects (74 male and 46 female) aged 25–55 years were taken. 60 subjects with normal fasting glucose (NFG) group, age and gender matched 60 subjects of impaired fasting glucose (IFG) group were recruited for this study. According to WHO (2006)[14] "NFG group is fasting plasma glucose <6.1 mmol/L and 2hour plasma glucose <7.8 mmol/L and IFG group is fasting plasma glucose 6.1 to 6.9 mmol/L and 2hour plasma glucose <7.8 mmol/L". Variables were age, waist circumference (WC), body mass index (BMI), blood pressure (BP), fasting plasma glucose (FPG), serum GGT and lipid profile. Data were analyzed with the help of SPSS version 23. Unpaired student's t-test, Pearson's correlation coefficient analysis and chi-square test were done. Odds Ratio (OR) and (95% CI), multiple regression analysis for relationship between FPG and serum GGT was performed. The *p*-value of <0.05 was considered statistically significant.

## Results

In this study it was observed that mean (±SD) of age (years), WC (cm), BMI (kg/m$^2$), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg), FPG (mmol/L), serum GGT (U/L), total cholesterol (TC) mg/dl, triglyceride (TG) mg/dl, low density lipoprotein cholesterol (LDL-C) mg/dl were significantly ($p$<0.01) higher in IFG than NFG.

In this study, Pearson's correlation analysis of FPG with serum GGT in all subjects (r=0.776, $p$<0.01) as well as IFG (r=0.435, $p$<0.01) showed significant correlation. It was evident from the study that, out of 120 subjects 54 IFG subjects had serum GGT levels >46.0 U/L indicating significant association ($p$<0.01) of serum GGT with IFG. Odds Ratio (OR) and (95%CI) for the association of serum GGT tertile with IFG where lowest tertile was considered as reference category T1 (< 24.0) U/L, which shows OR for T2 (24.0-42.0) U/L and T3 (>42.0) U/L is 4.12 and 20.25 respectively. It indicates that risk of developing IFG for T2 and T3 is 4.1 and 20.3 times higher than T1.

Multiple regression analysis of the relationship between FPG and serum GGT showed that adjusted $R^2$ was 0.707. Moreover, a significant association of FPG with WC ($p$<0.01) and serum GGT ($p$<0.01) were revealed through this analysis.

**Table-I:** Baseline characteristics and biochemical parameter of the study subjects (n=120)

| Variables | NFG group (n=60) | IFG group (n=60) | p value |
|---|---|---|---|
| Age (years) | 43.8±8.7 | 45.9±8.1 | 0.174 |
| BMI (kg/ m$^2$) | 22.7±1.4 | 28.4±2.3 | <0.01 |
| WC (cm) | 80±5.3 | 93.4±4.2 | <0.01 |
| SBP (mmHg) | 110.8±13.3 | 129.7±7.4 | <0.01 |
| DBP (mmHg) | 72.1±9.1 | 84.3±6.3 | <0.01 |
| FPG (mmol/L) | 4.4±0.8 | 6.5±0.3 | <0.01 |
| GGT (U/L) | 24.2±8.4 | 67.2±14.4 | <0.01 |
| TC (mg/dl) | 174.6±13.2 | 194.7±20 | <0.01 |
| TG (mg/dl) | 137.9±10.3 | 185.6±10.3 | <0.01 |
| HDL-C (mg/dl) | 45.5±3.4 | 36.2±4.3 | <0.01 |
| LDL-C (mg/dl) | 101.1±15.4 | 121.6±20.9 | <0.01 |

Unpaired Student's t-test was performed to compare between two groups.

**Table-II:** Multiple regression analysis of the relation between FPG and serum GGT by adjustment of other factors

| Variables | (R2=0.707) | |
|---|---|---|
| | β | P value |
| **Gender** | 0.103 | 0.111 |
| **Age** | 0.008 | 0.892 |
| **BMI** | 0.030 | 0.764 |
| **WC** | 0.282 | <0.01 |
| **SBP** | 0.127 | 0.185 |
| **DBP** | 0.007 | 0.936 |
| **TC** | 0.678 | 0.118 |
| **TG** | 0.056 | 0.794 |
| **HDL-C** | -0.206 | -0.241 |
| **LDL-C** | 0.753 | 0.102 |
| **GGT** | 0.324 | <0.01 |

## Discussion

The study revealed that, WC and BMI were significantly higher in the subjects of IFG group than in the subjects of NFG group. It suggests involvement of abdominal obesity in subjects of IFG. Similar result was observed by Wu et al[2]. Increased fat in the body promotes deposition of fat in the liver. Thus, hepatic insulin resistance is induced. It causes triggering of systemic insulin resistance. Thereby, IFG is developed[15]. There are also some other pathophysiological mechanism. One of them might be, obesity is a chronic inflammatory condition. In mitochondria, this inflammatory condition causes releasing of reactive oxygen species. Consequently, oxidative stress is occured[16]. It ultimately results a higher level of serum GGT. It has anti-oxidative stress

property. Finally, it causes damage of the liver; and damage of various tissues which are insulin-sensitive[2].

Serum GGT has an important role in the intracellular antioxidant defense. Lee et al. suggested that, oxidative stress could be involved in the development of prediabetes[17]. Pancreatic β-cells are vulnerable to oxidative stress. β-cells consist of reduced level of reactive oxygen intermediate scavenging enzymes, which are superoxide dismutase, catalase, glutathione peroxidase, etc[18]. Oxidative stress causes impaired insulin release from β-cells of pancreas[19]. In a study, it was found that, persons who progressed from Normal glucose tolerance to IFG within 5 years were characterized by a stationary, constitutive defective β-cells function or chronic reduced β-cells mass[20].

The study showed that IFG subjects had significantly more serum GGT than the NFG subjects. In this study, OR (95% CI) for tertile 3 was higher than tertile 2. Tertile 1 was taken as reference, which indicates that subjects with more serum GGT levels are at higher risk of developing IFG. These results are consistent with other studies[2,15]. Risk for IFG and T2DM increases with higher serum GGT, which was observed in a study conducted by Nakanishi et al[15]. The likely reasons for the associations between GGT and IFG may be as follows: increased serum GGT level is often associated with dyslipidemia and habits of adverse eating in adults. The association of higher serum GGT with IFG indicates greater risk of prediabetes. This suggests that increased levels of serum GGT may indicate early warning of diabetes, which needs prompt interventions to prevent diabetes[2].

In the present study, serum GGT was significantly higher in male than female among IFG subjects. Similar results were revealed in the studies of Wu et al[2] and Lee et al[17]. In this study positive correlation of FPG with serum GGT was evident among all subjects as well as IFG group but not in healthy NFG groups. No gender variation was found in these relationships. This suggests that elevation of GGT in the blood were related with an increased risk of IFG irrespective of gender[2]. These findings were consistent with the study conducted by Jun-hui et al[9].

In Multiple regression analysis of the relationship between FPG and GGT showed that adjusted $R^2$ was 0.707. It showed a direct association of IFG with WC ($p$<0.01) and serum GGT ($p$<0.01). Thus, it may be said that an elevation of serum GGT may be considered as an independent factor in the process of IFG development in our population. The result of the study coincides with the study of Nakanishi et al[15].

## Conclusion

In conclusion, it may be said that subjects with IFG have higher serum GGT than NFG subjects and higher serum GGT level is associated with greater risk of IFG. Moreover, GGT has strong independent relationship with FPG. The association of serum GGT with IFG suggests that it can be used as adjuvant marker for risk assessment of DM and screening tool for economically underdeveloped country like Bangladesh.

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