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Elevation in plasma gamma glutamyltransferase in gestational diabetes mellitus

Abstract

Gestational Diabetes Mellitus (GDM) is a complex metabolic disorder resulting in adverse effect of both maternal and fetal outcome. Oxidative stress plays an important role in the pathophysiology of GDM owing to inducing insulin resistance in the peripheral tissue and impairing insulin secretion from pancreatic β-cell. Oxidative stress is the condition of increased free radical activity and high lipid oxidation. GGT may be used as an indicator of the GDM. High level of GGT is emerging as a new risk factor for metabolic syndrome, which is cheap, rapid and easily available parameter for monitoring the patients with GDM. In this study, we enrolled 66 patients divided into two groups; GDM and normal pregnant women each having 33 subjects. We measured GGT and established its relationship with various parameters. The mean age of difference between two groups was statistically not significant ($p>0.05$). Chi-square test showed association of family history of diabetes mellitus were 27.27% and 6.06%, respectively in GDM and normal pregnancy group, which was statistically significant ($p<0.05$). Pearson's Correlation coefficients were 0.38, 0.57, 0.11, 0.46 between GGT and fasting blood sugar (FBS) 2hr PG after 75g oral glucose tolerance test (OGTT) and age. Our study revealed that GGT is higher in GDM group than in normal pregnancy group. It has also positive correlation with FBS and 2hr PG after 75g OGTT. Therefore, it can be used as an indicator of GDM and also monitoring these patients for metabolic syndrome.

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Introduction

Gestational Diabetes Mellitus (GDM) is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy".[1,2] Diabetes Mellitus (DM) diagnosed during pregnancy that is not clearly overt DM. This condition includes women whose glucose tolerance will returns to normal after pregnancy.[3] The high prevalence of GDM is increasing globally and 3% to 25% of total pregnancies may be affected by it.[3]

The incidence of GDM in primigravida of Bangladesh is 13.7% and out of this 12.5% found in first trimester 31.2% in 2nd trimester and 56.3% in 3rd trimester.[4] Oxidative stress plays an important role in the pathophysiology of GDM[5] Serum Gamma Glutamytransferase (GGT) plays an important role in oxidative stress and recently it has been recognized as a marker of oxidative stress.[6] There is a link between pre-gravid liver enzyme level and risk of GDM during a subsequent pregnancy and highest quartile of GGT level was associated with a twofold increased risk of subsequent GDM.[7]

Moreover, elevated GGT is strongly associated with obesity and excess deposition of fat in the liver termed non-alcoholic fatty liver disease which is thought to cause of hepatic insulin resistance and contribute to the development of systemic insulin resistance which is implicated in the pathogenesis of type2 DM (T2DM).[8,9] So far, my knowledge there is no such study in our country regarding this topic.

Materials and method

Study design

Cross sectional

Duration of study

March, 2014 to February, 2015

Place of the study

This study was conducted at the department of Clinical Pathology in collaboration with the department of Obstetrics and Gynecology, BSMMU, Dhaka.

Study population

Diagnosed case of GDM as per WHO criteria and comparable with normal pregnant women as control. WHO criteria[2] for diagnosis of GDM: Fasting blood sugar ≥7.0mmol/L, 2hour blood glucose after 75g OGTT ≥7.8mmol/L. Total sample size was 33x2=66

Sampling technique

Purposive sampling was used. The particulars of the patients and clinical data were recorded in a pre-designed data-sheet and kept until the end of the study. The whole procedure was explained to the participants and informed written consent was taken.

Patient selection

Patients were selected as per inclusion criteria from the obstetrics & gynecology outdoor as well as indoor. GDM (Gestational Diabetes Mellitus) patients were labeled as Group I and normal control as group II. In Group I, 33 patients and in Group II, 33 controls were selected.

Inclusion criteria

a. Diagnosed case of GDM as per criteria of WHO[2] as case.

b. Comparable normal pregnant women as control.

Exclusion criteria

i. Previous diagnosis of DM

ii. Pre-eclampsia

iii. Women with systemic disease, Collagen tissue disease, Heart disease, Renal disease, Chronic liver disease)

iv. Alcohol and some drugs that affects GGT (Phenytoin, Phenobarbital, Acetaminophen, HMG CO reductase inhibitor

Laboratory assay

Gamma Glutamyl Transferase concentration (GGT)

Fasting blood sugar

Prandial blood glucose-2hours after 75g oral glucose tolerant test (2hr PGOGTT)

Study procedure

Consent taken from patients

↓

First sample collected from GDM group and normal pregnant women group

↓

Reports of FBS and 2hr PGOGTT collected from patient's file

↓

Serum was separated and stored in -20◦c temperature

↓

Then GGT were measured by Siemens Dimension Max

↓

Analysis was done by SPSS (17)

Data collection

Data were collected by a predesigned preformat. Patient information was obtained through using patient's information sheet which involves, questionnaire, clinical finding & lab reports. Prior to the commencement of this study, the Ethical Institutional Review Board (IRB) of BSMMU, Dhaka, approved the research protocol. Universal precaution was maintained using gloves, lab coat and safety glasses were worn when handling all human blood products and infectious viruses. Disposable plastic, glass, paper and gloves that contact blood were placed in a biohazard bag or discard autoclaved. Disinfection of all working surface was done with 10% bleach solution. Other potentially contaminated materials were disposed in a biohazard bag. Other non-disposable materials were disinfected at the end of working day. Hands were washed thoroughly after removal of personal protective devices used in handling specimens and kit reagents.

Result

A total of 66 patients were included in this study. They were divided into three sub-groups according to age. The mean age of the patients with GDM (group I) was 26.69±4.60years and range were 20-36years. The mean age of the normal healthy pregnant women (group II) was 26.87±6.57years and range was 17-40years. The maximum age of groups was 21-30years in Group-I and Group-II which was 72.73% and 57.58% respectively. Unpaired "t" test showed that mean age of this two groups were similar with no significant difference (p >0.05) (Table 1).

Table 1 Age group distribution of the study population (n=66)

Age(in year)	Study group		Total	p value
	Group-I	Group-II		
< 20years	02(6.06)	06(18.18)	8	
21-30years	24(72.73)	19(57.58)	43	
31-40years	07(21.21)	08(24.24)	15	
Total	33(100)	33(100)	66	
Mean±SD	26.69 (±4.60) 20-36yrs	26.87 (±6.57)17-40yrs		0.89NS

*Unpaired "t" Test was done to measured the level of significance

S, significant; NS, not significant; Group-I, GDM; Group-II, normal pregnancy

The mean gestational age of women with GDM and with normal control were 34.78(±2.63) (range 30-39) and 35.90(±1.97) (range 30-38) respectively. Unpaired "t" test showed the age (weeks) was not statistically significant (p=0.05) (Table 2).

Table 2 Comparison of mean gestational age (weeks) in the study patients (n=66)

	Study group		p value
	Group-I	Group-II	
Mean Gestational age(Weeks)	34.78(±2.63)	35.90(±1.97)	0.05NS
Range(Min-max)	30-39(weeks)	30-38(weeks)	

*Unpaired "t" Test was done to measured the level of significance

NS, not significant: Group-I, GDM; Group –II, normal pregnancy

Figure 1 showed significant a positive correlation between FBS and GGT level in GDM group, Pearson Correlation value was 0.35 that means 35% possibility when GGT increased than FBS increased, which was statistically significant (p<0.05)

Figure 2 showed significantly a positive correlation between FBS and GGT levels in normal pregnancy group. Pearson Correlation value was 0.07 that means 07% possibility when GGT increased than FBS increased which was statistically not significant (p>0.05).

Figure 3 showed a significant positive correlation between 2hs PBOGTT and GGT level in GDM group, Pearson Correlation value was 0.42 that means 42% possibility when GGT increased than 2hs PGOGTT level increased, which was statistically significant (p<0.05).

Figure 4 showed significantly a positive correlation between 2hs PGOGTT and GGT level in normal pregnancy group, Pearson

Correlation value was 0.22% that means 22% possibility when GGT increased than 2hs PGOGTT level increased, which was statistically not significant (p>0.05).

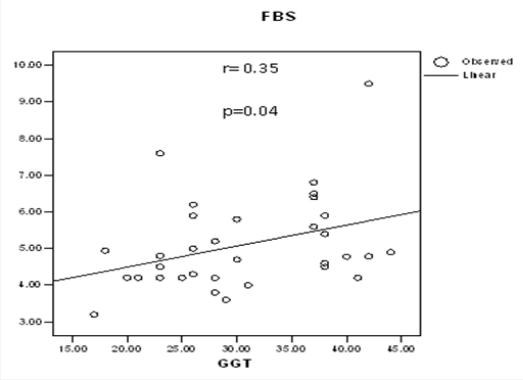

Figure 1 Correlation between FBS and GGT in GDM group.

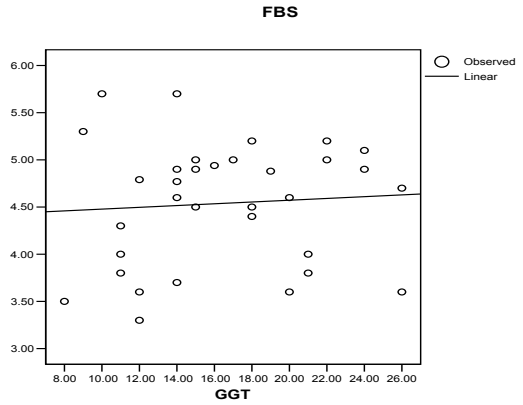

Figure 2 Correlation between FBS and GGT in normal pregnancy group.

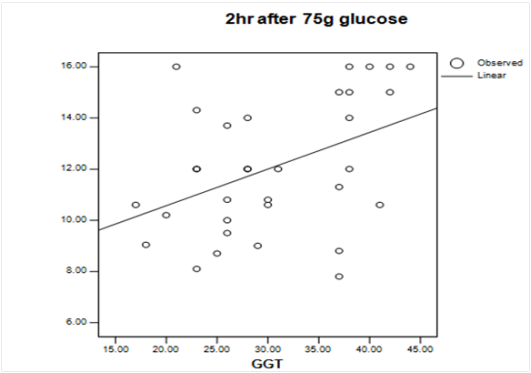

Figure 3 Correlation between 2hr PGOGTT and GGT in GDM group.

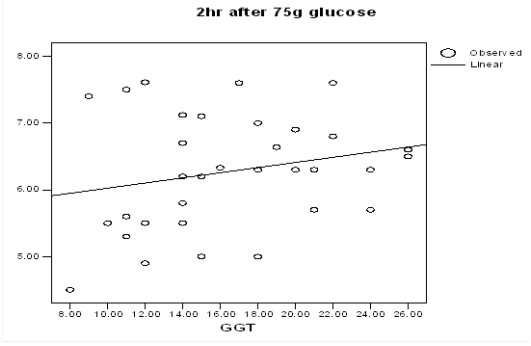

Figure 4 Correlation between 2hr PGOGTT and GGT in normal pregnancy group.

Figure 5 shows a correlation between age in years and GGT. Pearson Correlation value was 0.11 that means 11% possibility when age in years increased than GGT increased, which was not statistically significant.

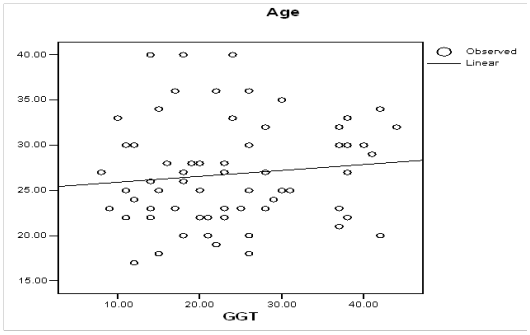

Figure 5 Correlation between ages in years and GGT.

The mean level of GGT was 30.60±7.78(range 17-44) in women with GDM and 16.45±4.97 (range 8-26) in normal pregnant women (p<0.05). Mean FBS level was 5.10(±1.26) in GDM group and 4.53(±0.65) in normal pregnancy group (p<0.05). Mean 2hs PGOGTT level was 9.75(±1.52) in GDM group and 6.27(±0.85) in normal pregnancy group (p<0.05). The FBS and 2hs PGOGTT and GGT in GDM group were significantly higher than in normal group when compared by unpaired "t" test (p <0.05). (Table 3)

Table 3 Comparison of FBS and 2hs PGOGTT and GGT levels in study population

	Study group		
	Group-I	**Group-II**	**p value**
FBS (mmol/L)	5.10 (±1.26)	4.53 (±0.65)	0.02S
Range(Min-max)	3.20-9.50	3.30-5.70	
2hr PGOGTT after 75g glucose(mmol/L)	9.75(±1.52)	6.27(±0.85)	<0.001S
Range(Min-max)	7.80-14.30	4.50-7.61	
GGT(U/L)	30.60 (±7.78)	16.45 (±4.97)	<0.001S
Range(Min-max)	17-44	26-Aug	

*Unpaired "t" test was done to measure the level of significance, S, significant

Table 4 shows a significant relation of GGT in GDM and normal pregnancy groups. Most of 93.94% in GDM group were GGT ≥19.5U/L (p<0.001) which was statistically significant.

Table 4 GGT values in GDM group and normal pregnancy group of the study population (n=66)

GGT	Study group		Total numbers participated	p value
	Group I	**Group-II**		
< 19.5U/L	02(6.06)	23(69.70)	25	< 0.001S
≥19.5U/L	31(93.94)	10(30.30)	41	

Chi-square tests S, Ssignificant

The test results variable (s)

GGT (0.94) has at least one tie between the positive actual state group and the negative actual state group. Ninety five % confidence interval of the difference was lower -0.889 and upper -0.991. The test results variable(s): GGT (0.94) has at least one tie between the positive

actual state group and the negative actual state group. Sensitivity was 98% and specificity was 50%. Ninety five % confidence interval of the difference was lower -0.889 and upper -0.991. Cut off value was 19.50 (Figure 6).

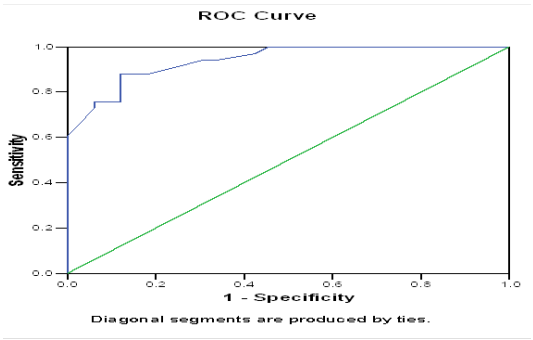

Figure 6 Receiver-operator characteristic curves of GGT in group-I (GDM).

Discussion

The high prevalence of GDM is increasing globally and 3% to 25% of total pregnancy may be affected by it.[3] In this study, gestational age of GDM (Group I) was 30-39weeks and normal pregnancy (Group II) was 30-38weeks, which was statistically not significant (p>0.05).

Oxidative stress plays an important role in the pathophysiology of T2DM owing to inducing insulin resistance in the peripheral tissue and impairing insulin secretion from pancreatic β cell.[10,11] Serum GGT plays an important role in oxidative stress.[6] Elevated serum GGT levels are a reflection of high degree oxidative stress.[12] This suggests a relationship between the GDM and GGT is emerging as a new risk factor for prediction of GDM.[13] In our study, to observe association of serum GGT with GDM we enrolled 66 participants, among which 33 were GDM as cases and 33 were normal pregnant women as control.

Age is risk factor (>25years) in case of GDM. In our study the mean age of the patients with GDM (Group I) was 26.69±4.60years and range were 20-36years. The mean age of the normal healthy pregnant women (Group II) was 26.87±6.57years and range was 17-40years. The difference of mean age was not statistically significant among two groups (p >0.05). These findings are consistent with the findings of other studies.[7,14]

Sridhar SB et al.[7] and co investigators (2014) showed that the mean age of GDM were 28.26±5.5years and 28.46±5.2years were in control that is similar to our study. Also the differences in age between the groups were statistically not significant (p>0.05). In our study, the mean levels of GGT were 30.60±7.78(range 17-44) in women with GDM and 16.45±4.97(range 8-26) in normal pregnant women. The mean levels of GGT of GDM were higher than normal control that was statistically highly significant (p<0.05). In the receiver operator characteristic curve analysis, cutoff value of GGT was set at 19.50; sensitivity was calculated 98% and specificity was 50%.This result is similar to other studies.[7,13,14,15] The study conducted by Endogan S et al.[13] showed that GGT in the GDM group were higher than normal control, which was statistically significant (p<0.05). In another study, conducted by Alanby I et al.[15] showed that cut off value of GGT was 16 IU/L the sensitivity was 86% and specificity was 37%. This is approximately similar to our study.

In this study, the mean GGT values were higher in the GDM group than normal control. A study conducted by Tan PC et al.[14] showed that cut off value of GGT was 24IU/L. In such study, raised GGT had a sensitivity of 23.2% and specificity of 86.1% .This sensitivity and specificity are not similar with our study. The probable reason used GGT as a diagnostic marker. Sridhar SB et al.[7] showed that the mean levels of GGT were 28±21.7 U/L in GDM group and 22±16.6U/L in normal control group respectively, which was statistically highly significant (p<0.05).

In present study, mean levels of FBS were 5.10(±1.26)mmol/L in GDM group and 4.53(±0.65)mmol/L in normal pregnancy group, respectively (p<0.05). Mean levels of 2hr after 75g glucose OGTT were 9.75 (±1.52) mmol/L in GDM group and 6.27(±0.85)mmol/L in normal pregnancy group respectively (p<0.05). The FBS 2h after 75g glucose and GGT in GDM group were significantly higher than in normal group. This study showed significantly a positive correlation between FBG and GGT levels in GDM group.

Pearson Correlation value was 0.35 that means 35% possibility when GGT increased than FBS increased. In normal pregnancy group, there was also positive correlation of FBS and GGT. Pearson Correlation value was 0.07 but there was statistically not significant (p>0.05). Tan PC et al.[14] conducted a study showed GGT was not positively correlated with FBS (Spearman's rho=0.067: p>0.05). This is contradicted with present study. In the present study, significantly a positive correlation was seen between 2hr PGOGTT and GGT in GDM and normal pregnancy groups.

In GDM group, Pearson Correlation value was 0.42 that means 42% possibility when GGT increased than 2hr PGOGTT increased that was statistically significant(p<0.05). In normal pregnancy group, Pearson Correlation value was 0.22, which was statistically not significant. Tan PC et al.[14] study showed positive correlation between 2hs PGOGTT and GGT values. These results were consistent with our results. Association was found between GDM and GGT which was statistically significant (p<0.05). No other study shows this association.

Conclusion

Our study showed that GGT was higher in GDM group than normal control .We also found that increase in FBS and 2PGOGTT were directly proportional to increase GGT. Hence, it may be used as a risk factor for GDM and monitoring of metabolic syndrome. We propose that GGT can be used as a simple and cost effective tool for monitoring and prevention of complications in the women with GDM.

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None.

Conflict of interest

Author declares that there is no conflict of interest.

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