Original Article

Gamma-glutamyl transferase is an indicator of gestational diabetes mellitus

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Abstract

Increased gamma-glutamyl transferase (GGT) is associated with gestational diabetes mellitus (GDM) and type 2 diabetes mellitus in pregnant women. This cross sectional study was conducted in the Department of Clinical Pathology in collaboration with Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from March 2014 to February 2015 to assess the GGT as an indicator of GDM. Total 66 pregnant women were enrolled in this study in the Department of Obstetrics and Gynecology, BSMMU. Total 33 cases were considered as Group I (GDM) and 33 controls were Group II (normal healthy pregnant women). Two ml of blood was collected in plain test tube from each patient. Gestational diabetes mellitus were diagnosed by FBS and 2hr after 75g glucose in this study as cases. Normal healthy pregnant women was included in this study as control. GGT was higher in GDM group compared to normal healthy pregnant women (30.60±7.78 vs. 16.45±4.97, p<0.001). So, with the help of GGT we can take preventive measure and precaution to reduce the risk of GDM in pregnant women.

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Key words: Gamma-glutamyl transferase(GGT), gestational diabetes mellitus(GDM), pregnancy, liver enzyme

Introduction

Gestational diabetes mellitus is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy"[1,2]. This condition includes women whose glucose tolerance will return to normal after pregnancy and those who will persist with glucose intolerance and type 2 Diabetes Mellitus.[3] It is the most common medical problem and metabolic complication in pregnancy and 3% to 25% of total pregnancies may be affected by GDM.[3] The incidence of GDM in primi- gravida of Bangladesh is 13.7% and out of this 12.5% found in first trimester, 31.2% is in second trimester and 56.3% in third trimester.[4]

GDM is associated with adverse pregnancy outcomes and the subsequent development of diabetes in mothers. [5, 6, 7] Pregnancy is a complex metabolic endocrine process. Insulin resistance usually begins in the second trimester of pregnancy and progress throughout the pregnancy. On the basis of this, screening is done on 24th to the 28th weeks of gestation.[8] Normal glucose tolerance in early pregnancy does not exclude the risk of development of GDM later.Oxidative stress plays an important role in the pathphysiology of GDM.[9]

Serum gamma glutamyl transferase plays an important role in oxidative stress and recently it has been recognized as a marker of oxidative stress.[10] Gamma-glutamyl transferase (GGT) is an ectoplasmic enzyme responsible for the extracellular catabolism of glutathione (GSH). The enzyme is produced in many tissues, but mainly derived from liver.[11] There is a link between pre-gravid liver enzyme level and risk of gestational diabetes during a subsequent pregnancy and highest quartile of GGT level was associated with a twofold increased risk of subsequent GDM.[12] Oxidative stress is the condition of increased free radical activity and high lipid oxidation. It plays a role in etiology of type 2 diabetes by inducing insulin resistance in the peripheral tissue and impairing insulin secretion from pancreatic β-cell.[13,14]

Elevated GGT is strongly associated with obesity and excess deposition of fat in the liver, termed as non-alcoholic fatty liver disease. It is thought to caused by hepatic insulin resistance and contribute to the development of systemic insulin resistance which is

implicated in the pathogenesis of type 2 DM.[15] There are some hematological and biochemical predictor for GDM i.e. GGT, ALT, PCT (plateletcrit), PDW (platelet distribution width) adioponectin, follistatin like-3, sex hormone binding globulin.[16,17] ALT is a marker for liver fat accumulation and is more specific for liver pathology.[12] Other than liver, GGT is also found in other tissues and is less specific for liver pathology.[18] PCT, PDW is measured by modern hematological auto analyzer which is not available in all the areas of our country. Adioponectin, Follistatin like-3, sex hormone binding globulin is very expensive test and not available in rural areas or all the centers of our country.

On the other hand, measurement of GGT is simple, automated, cheap and easy to carry out. So, for the assessment of risk of gestational diabetes mellitus, this test may be used as an alternative screening method for GDM that does not require glucose ingestion and waiting for a blood sample that is more hazardous for the patient. It can be used for predicting the possibility of type 2 DM. GGT may help to identify risk group women who would benefit from interventions during the early pregnancy period.

Methods

This cross sectional study was conducted in the Department of Clinical pathology , in collaboration with the Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from March 2014 to February 2015. Total 66 pregnant women were enrolled in this study. Among them, 33 pregnant women with GDM were considered as Group I and 33 normal pregnant women with out GDM were were Group II and considered as controls.

Previous diagnosis of DM, pre-eclampsia, pregnant women with systemic disease (HTN, onnective tissue disease, heart disease, renal disease, chronic liver disease), history of taking alcohol and some drugs that affects GGT (Phenytoin, phenobarbital, acetaminophen) were excluded from the study. In this study patients' gamma glutamyl transferase were measured by biochemistry auto analyzer (Simens Dimension Max) in the Department of Clinical Pathology, BSMMU.

After selection, all the patients were thoroughly informed about the aims, objectives and procedure of the study. An informed written consent was taken from each subject. Detailed personal, medical and educational history, gestational weeks, family history of DM, previous history of GDM, para and gravida were recorded. Thorough physical examinations were done and documented. Gamma glutamyl transferase was measured by biochemistry auto analyzer. Fasting plasma glucose, plasma glucose 2 hours after 75 g glucose were also done.

Results

A total of 66 patients were included in the study. 33 cases were considered as Group I (GDM) and 33 control were considered as Group II (normal pregnancy). The mean age of the GDM (Group I) was 26.69 (±4.60) years; the mean age of the patients having normal pregnancy (Group II) was 26.87 (±6.57) year**.**

The gestational age of women with gestational diabetes mellitus and normal control were 34.78(±2.63) weeks and 35.90(±1.97) weeks respectively. Unpaired "t" test showed that difference of gestational age(weeks) among two groups was not statistically significant(p=0.05). (Table-I)

Table I: Comparison of gestational age (weeks) of the study patients (n=66)

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

*Unpaired"t" Test was done to measured the level of significance; S=Significant, NS=Not significant, Group-I = GDM, Group –II= Normal pregnancy

Significant positive correlation between GGT and fasting blood glucose level in GDM group was found. Pearson correlation value was 0.35(p< 0.05), that means there is 35% possibility that FBS increases when GGT is increased. (Figure-1)

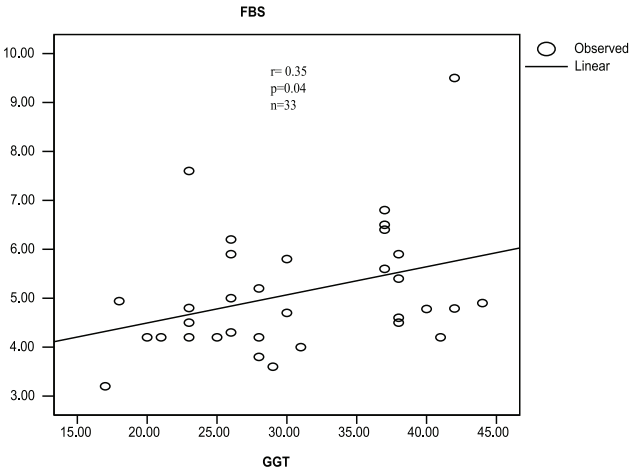

Figure-1: *Correlation between GGT and FBS in GDM group (n=33)*

Significant positive correlation between GGT and fasting blood glucose level in normal pregnancy group was found. Pearson Correlation value was 0.07(p> 0.05), that means there is 7% possibility that FBS increases when GGT is increased; but it was statistically not significant (p 0.05). (Figure-2)

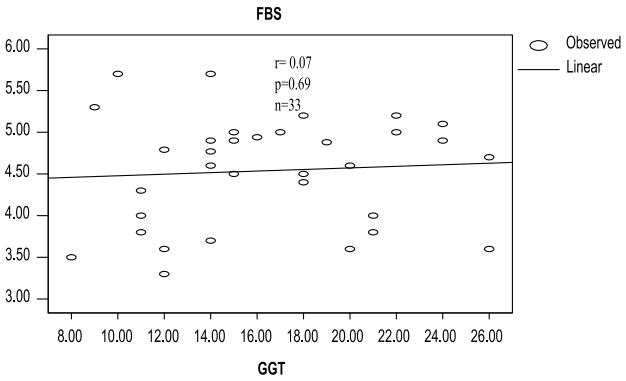

Figure-2 : *Correlation between GGT and FBS in normal pregnancy group (n=33)*

The mean GGT were 30.60±7.78 (range 17-44) U/L in women in GDM group and 16.45±4.97 (range 8-26) U/L in normal pregnant women. Mean FBS was 5.10(±1.26) mmol/L in GDM group and 4.53(±0.65) mmol/L in normal pregnancy group (p<0.05). Mean 2hr after 75g glucose was 9.75(±1.52) mmol/L in GDM group and 6.27(±0.85) mmol/L in normal pregnancy group (p<0.05). Mean GGT was 30.60(±7.78) U/L in GDM group and 16.45(±4.97) U/L in normal pregnancy group (p<0.05). The FBS, 2h after 75g glucose and GGT of GDM group were significantly higher than normal group when compared by unpaired "t" test (p <0.05). (Table-II)

Table II : Comparison of FBS, 2h after 75g glucose and GGT among study population (n=66)

		Study group		
		Group-I	Group-II	p value
FBS		5.10(±1.26)	4.53(±0.65)	0.02[S]
	Range	3.20-9.50	3.30-5.70	
2hr after 75g glucose		9.75(±1.52)	6.27(±0.85)	<0.001 [S]
	Range	7.80-14.30	4.50-7.61	
GGT		30.60(±7.78)	16.45(±4.97)	<0.001 [S]
	Range	17-44	8-26	

Unpaired "t" test was done to measure the level of significance; S=Significant

GGT was high among most of the cases of GDM (93.94%) compared to 30.30 % of normal pregnancy. This relation between GGT with GDM was statistically significant. (Table-III)

Table III: Association between GGT with GDM of the study population (n=66)

GGT	Study group		Total	p value
	GDM	Normal pregnancy		
< 19.5 U/L	02(6.06)	23(69.70)	25	
≥19.5 U/L	31(93.94)	10(30.30)	41	< 0.001[S]
Total	33(100)	33(100)	66	

Chi-Square Test

Discussion

The high prevalence of GDM is increasing globally and 3% to 25% of total pregnancy may be affected by GDM.[3] It is the most common metabolic complication in pregnancy. Serum GGT remains normal during pregnancy.[19] In our study gestational age of GDM (Group I) was 30-39 weeks and in normal pregnancy (Group II) it was 30-38 weeks. This difference was statistically not significant (p<0.05). GDM and type 2 diabetes mellitus share several risk factors and the incidence of GDM reflects the prevalence of type 2 diabetes mellitus.

Age (>25 years) is a risk factor in case of GDM.[4] In our study the mean age of the patients with GDM (Group I) was 26.69± 4.60 years and range were 20-36 years. The mean age of the normal healthy pregnant women (Group II) was 26.87±6.57 years and range was 17-40 years. The difference of mean age was not statistically significant among two groups (p>0.05). This findings are consistent with the findings of other studies.[12,20] Sridhar SB and co-investigators showed that the mean age of GDM was 28.26±5.5 years and the mean age of control was 28.46±5.2. These findings were similar to our study.

In our study, mean FBG were 5.10 (±1.26) mmol\L and 4.53(±0.65)mmol\L in GDM group & normal pregnancy group respectively. Mean value of blood glucose 2hr after 75g glucose were 9.75(±1.52) mmol\L in GDM group and 6.27(±0.85)mmol\L in normal pregnancy Group (p<0.05). The FBG, 2h after 75g glucose and GGT of GDM group were significantly higher than normal pregnancy group when compared by unpaired "t" test (p<0.05).

Our study showed significant positive correlation between GGT with fasting blood glucose level in GDM group. Pearson correlation value was 0.35 ($p < 0.05$) that means there is 35% possibility that FBS increases when GGT is increased. In normal pregnancy group, there was also positive correlation between GGT & FBG and pearson correlation value was 0.07. But it was statistically not significant ($p > 0.05$).

Receiver operator characteristic curve analysis shows that, cutoff value of GGT was set at 19.50, sensitivity was calculated 98% and specificity was 50%. This result is similar to other studies.[12,16,21,22] Another study showed that GGT in the GDM group were higher than normal control & that was statistically significant ($p < 0.05$).[16] Other study showed that cut off value of GGT was 16 IU/L, the sensitivity was 86%, and specificity was 37%.[22] This is approximately similar to our study.

In our study the mean GGT values were higher in the GDM group than normal control. A study showed that cut off value of GGT was 24IU/L.[21] In this study, raised GGT had a sensitivity of 23.2% and specificity of 86.1%. This sensitivity and specificity is not similar with our study. The probable reason was that, they also used GGT as a diagnostic marker. Sridhar SB et al showed that the mean GGT were 28±21.7 U/L & 22±16.6 U/L in GDM group and in normal control group respectively; it was statistically highly significant ($p < 0.05$).

Our study showed that GGT was higher in GDM group than normal control. Significant positive correlation was found between GGT with FPG and 2hr after 75g glucose. GGT can be used as a simple and cost effective indicator for identification of risk group women for GDM and earlier prevention of the GDM in pregnant women.

This study was done in a limited span of time. The main limitation of our study was the small sample size and this was a non-randomized single center study. All the confounding variables influencing GGT were not investigated extensively.

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