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Clinical Biochemistry

GAMMA-GLUTAMYL TRANSFERASE IS AN INDICATOR OF GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Introduction: The insulin resistance of pregnancy provides a unique stress test for life for women. Gestational diabetes mellitus (GDM) is a global health concern, not only because its prevalence is high, but also because of the potential implications for the health of mothers and their offspring.

Objective: The aim of this study was to evaluate plasma gamma-glutamyl transferase (GGT) in gestational diabetes mellitus (GDM) in pregnant women.

Methods: The study group comprised 702 pregnant patients with and without GDM (232 women with GDM and 470 normal pregnant women). Serum fasting glucose, 50g-oral glucose challenging test (OGCT) and liver enzyme like GGT were measured for all.

Results: The GDM group had significantly higher mean GGT activities than the healthy controls. Conclusion: GGT was higher in the GDM group than the control group. Our findings suggest that GDM risk increases substantially with increasing maternal BMI.

KEYWORDS : GDM, OGCT, GGT

INTRODUCTION

Gestational diabetes mellitus (GDM) is a global health concern, not only because its prevalence is high and on the increase, but also because of the potential implications for the health of mothers and their offspring. They are likely to have large babies and subsequent delivery complications. GDM 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 tolerance are Type 2 diabetes mellitus [3, 4]. GDM develops in 1-3% of all pregnancies. GDM not only influences immediate maternal (preeclampsia, stillbirths, macrosomia and need for caesarean section) and neonatal outcomes (hypoglycaemia, respiratory distress); but also increases the risk of future Type 2 diabetes in mother as well as the baby. A recent meta-analysis showed that women with gestational diabetes have a greatly increased risk of developing Type 2 diabetes. Women with GDM are characterised by a relatively diminished insulin secretion coupled with pregnancy induced insulin resistance located in skeletal muscle tissue. Insulin resistance and inadequate insulin response are two known mechanisms underlying the pathophysiology of both GDM and Type 2 diabetes [4]. The liver is crucial in maintaining glucose homeostasis, both during fasting and postprandial states, and thereby plays a role in the development of type 2diabetes. Laboratory tests for Gamma Glutamyl Transferase (GGT), Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) are commonly performed to assess the overall health of the liver. Earlier researches suggests that during a normal pregnancy, liver enzyme levels may change in response to the increased insulin resistance induced by pregnancy [3, 5]; therefore, it is important to determine whether pre pregnancy levels of liver enzymes are related to subsequent risk of GDM, in order to clarify the temporal sequence of the association. Although liver enzymes are known to correlate with features of insulin resistance, a risk factor for the development of GDM, the relationship between pre pregnancy liver enzyme levels and GDM is unclear.

Oxidative stress plays an important role in the pathophysiology of GDM. Serum Gamma Glutamyl Transferase (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]. The objective of this study was to assess the potential role of liver enzyme (GGT) levels in predicting GDM.

MATERIALS and METHODS

Subjects: This cross sectional study comprised 702 pregnant patients with and without GDM (232 women with GDM and 470 normal pregnant women). We used the electronic data of patients of Chennai Medical College Hospital and Research Centre, Irungalur, Trichy, TN., who consulted during April 2016 to March 2016. The study participants were residents of in and around Trichy, Tamil Nadu, South India. The subjects were pregnant women clinically diagnosed as GDM during third trimester (28-40 weeks) with the age 18-40 years visiting obstetrics OPD and wards of our Hospital. Only electronic medical records (clinical and laboratory) of selected patients were extracted for the purpose of this study. Laboratory data included serum fasting glucose, 50g – Oral Glucose Challenging Test (OGCT) and liver enzyme like GGT. Diagnosed cases of GDM as per the criteria of WHO [8] are compared with normal pregnant women as control. We excluded women with liver diseases (e.g. Hepatitis B carrier status, NAFLD), pre-eclampsia, previous diagnosis of DM, women with collagen tissue disease, heart disease, renal disease, consumption of alcohol and some drugs that affects GGT (Phenytoin, Phenobarbital, Acetaminophen, HMGCOA- reductase inhibitor.

Fasting blood glucose, 2 hr - 50g oral glucose challenging test (OGCT) and GGT activity (with Gamma glutamyl p-nitroanalide as the substrate & Glycylglycine as the peptide acceptor) were estimated using Mindray BS-420 chemistry analyser.

Rate of Gestational Weight Gain per Week: The rate of gestational weight gain per week was calculated as follows: (weight measured at or before the glucose screening test - prepregnancy weight) / weeks of gestation attained at the time of the weight measurement.

Statistical Analysis: Descriptive data are presented as means and standard deviations (SD). Data analysis between two groups was compared using two-tailed independent sample t-test. Data were analysed using IBM SPSS statistics 20. $p < 0.005$ was considered as significant.

RESULTS

A total of 702 pregnant women were included in this study (232 women with GDM and 470 normal pregnant women). The mean gestational age of women with GDM and normal control were 34.78±2.63 and 35.90±1.97 weeks respectively. Unpaired "t" test showed the age (weeks) was not statistically significant (p=0.05). Women with GDM compared to those without were older, of higher

parity and with higher Body Mass Index (BMI). OGCT and GGT levels are higher in women with GDM.

Chi Square for trend analysis into quartiles showed a significant result for GGT. The relative risk (RR) of GDM for the highest GGT quartile was compared to the lowest GGT quartile which was statistically significant (P=0.039) (Table 1).

Table 1: Biochemical characteristics of selected antenatal women with and without gestational diabetes after the 50 g 2-hour Oral Glucose Challenge Test

	GDM (n = 232)	No GDM (n = 470)	P value
FBS (mg%)	150±09	95±10	< 0.005
2 hr OGCT After 50g glucose administration (mg%)	210±5.5	110±11	< 0.005
BMI (Kg/m^2)	30±6.5	23±3.5	< 0.005
GGT in U/L	30±7.78	11.45±4.37	< 0.005
GGT expressed as Quartiles:	37 (14.3)	117 (25.0)	Chi Square test RR (95% CI)
1st Quartile (< 10 U/L)			
2nd Quartile (11 - 14 U/L)	47 (18.4)	117 (25.0)	0.89 (0.66–1.21) P=0.893
3rd Quartile (15 - 20 U/L)	74 (28.9)	118 (25.0)	1.15 (0.87–1.55) P=0.322
4th Quartile (> 21 U/L)	74 (28.9)	118 (25.0)	1.35 (1.02-1.80) P=0.039

DISCUSSION

Statistically significant results are shown in our GDM women of a higher mean for their GGT concentration, a positive trend in the rate of GDM as GGT quartile band increased, a higher relative risk of GDM in the top versus bottom quartile GGT band. Raised GGT concentration on a number of bivariate analyses seems to be associated with GDM.

A recent review of 21 prospective population studies suggests that raised GGT maybe a better predictor for diabetes than raised ALT [9]. Our data in the context of GDM supports the above view, raised GGT is the better marker of a tendency to glucose intolerance in pregnancy.
The predictive value of GGT and ALT for development of type 2 diabetes is at least in part explained by their role as a surrogate for liver fat content and non-alcoholic fatty liver disease (NAFLD) which has a strong link to the pathogenesis of type 2 diabetes [10,11]. Our result could imply that NAFLD may not be as important an element in the pathophysiology of GDM.

Our study results suggest that GGT could be useful as predictors of pregnancies with the potential of developing GDM. In recent years, several studies have investigated the predictive value of liver enzymes and elevated GGT levels in particular have been found to be significantly correlated with impaired glucose tolerance [12, 13]. Other studies have demonstrated an increased risk of developing DM in the future in pregnant women with elevated ALT and GGT activities, and that liver steatosis and hepatic insulin resistance play a role in this process [13, 14]. Additionally, GGT has been shown to facilitate the stress response of the endoplasmic reticulum [15]. In our study, the GDM group had significantly higher mean GGT activities than the healthy controls. While our findings conflict with those of previous studies on patients with GDM [8], similar results have been reported in patients with DM [13].

Foetal growth is dependent on the capacity of mother to supply nutrients and also on the capacity of the placenta to transfer these nutrients to the foetus. Despite different diagnostic criteria, many studies confirmed that GDM increases the risk of macrosomia or LGA birth [17, 18]. Maternal hyperglycemia increases foetal growth via delivery of excess maternal plasma glucose to the foetus, which results in foetal hyperinsulinemia and promotes foetal overgrowth [19]. There was increasing risk of GDM as the quartile of GGT increased, and being in the highest quartile of GGT with a pre pregnancy BMI of 30 Kg/m^2 resulted in the greatest risk of GDM.

CONCLUSION

Our study showed that GGT was higher in GDM group than normal control. Our findings suggest that GDM risk increases substantially with increasing maternal BMI. Regardless, pregnancy may provide an opportunity for women to adopt lifestyle changes and other secondary prevention strategies, which may prevent progression of GDM.

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