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Original Research Article

A comparative and correlative study of serum homocysteine level in gestational diabetes mellitus and normal pregnancy

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ABSTRACT

Background: An alarming increase in Gestational diabetes mellitus (GDM) cases worldwide elevates concern regarding the consequences including fetal macrosomia, preeclampsia and many more. Plasma homocysteine levels which has direct impact on to endothelial function of blood vessels. The relationship of homocysteine and GDM is yet to be clarified.
Methods: This single centre prospective observational study was conducted in Department of Obstetrics and Gynaecology of Thanjavur medical college hospital among 50 pregnant primi and multi gravida patients with normal pregnancy and gestational diabetes mellitus to assess the association and comparison of serum homocysteine levels in both groups.
Results: The mean value of homocysteine in control group was 3.8 ± 0.95 and in gestational diabetes patients was 16.30±6.09. On comparison, found that there was hyperhomocysteinemia among GDM patients with normal pregnancy and results were statistically significant (T= -9.024 Df=48.000 <0.05).
Conclusions: In this comparative and correlative study, we found that patients with gestational diabetes mellitus have higher serum homocysteine levels in comparison with normal pregnant women. Hyperhomocysteinemia is found to be an independent risk factor for gestational diabetes mellitus patients. Further investigations are needed to follow up for these patients in the postpartum period and later in their life.

Keywords: Gestational diabetes mellitus, Glucose challenge test, Homocysteine, Hyperhomocysteinemia, Multigravida, Primigravida

INTRODUCTION

Currently burden of gestational diabetes is rising worldwide, which includes women with diabetes and intermediate hyperglycaemia with impaired glucose tolerance and blood sugar levels in pregnancy. Diabetes during pregnancy can be the cause of poor outcome not only for mother during pregnancy but also for the child who will have an increased risk of developing obesity and type 2 DM in the future.[1] Deleterious effects of homocysteine on endothelial function are explained in various studies. However, its relationships to and role in the onsets of GDM are unclear. Few studies have revealed Homocysteine is associated with increased insulin level in blood.

This is an attempt to increase supportive quality data regarding serum homocysteine level in GDM, the aim of this study is to study the association of serum homocysteine levels in gestational Diabetes mellitus and to compare the serum homocysteine levels in gestational diabetes mellitus and in normal pregnancy.

METHODS

Study site and design

This single center prospective observational study was conducted in Department of Obstetrics and Gynecology of Thanjavur medical college hospital from December 2013 to June 2014 and involved 50 inpatient women with normal pregnancy and also with GDM of both primi and multigravida.

Subjects

Out of 50 pregnant primi and multi gravida patients, 20 were of normal pregnancy and 30 newly diagnosed GDM with glucose challenge test and confirmed by Oral Glucose Tolerance Test (OGTT) as per WHO criteria and American Diabetes Association (ADA) criteria were included. Patients with DM type 1 and 2, coronary artery disease, chronic kidney disease and family history of diabetes mellitus are excluded. The study was conducted in accordance with regulations of Institutional Ethics Committee after the approval. Patients were estimated for serum homocysteine level with using Flurorescense Polarization Immuno Assay (FPIA). Other investigations like complete hemogram, Fasting and post prandial blood sugar (FBS, PPBS), renal function test, Lipid profile, Glucose challengetest, Oral Glucose tolerance test were conducted.

Statistical analysis

Data were using Mean±standard deviation (±SD), Range, Frequencies (number of cases) and relative frequencies (percentages) when appropriate. For comparing categorical data, Chi square (X^2) test was performed. The p value less than 0.05 was considered statistically significant by using the software SPSS for windows 14 evaluation version and conclusion were drawn.

RESULTS

Out of 50 patients were included in this study, 20 (40%) were as control group with normal pregnancy and 30 (60%) were newly diagnosis as gestational diabetes mellitus as test group. Among each group primi and multi gravida are equally distributed. Mean age group of control and gestational diabetes patients group in this study was 24.25 and 25.8 years.

Screening test of glucose challenge test done in all patients with 50 g of glucose and its values are statistically significant (T= -8.797 Df=48 .000<0.05) and details of results were explained in Table 1.

Table 1: Glucose challenge test in both groups.

GCT	Normal pregnancy group	GDM group
<140 mg /dl	17	00
140-160 mg /dl	3	17
>160 mg /dl	0	13
Mean	114.50	162.42
Std deviation	20.87	17.46

After glucose challenge test, oral glucose tolerance test (after overnight fast with 100 gm of glucose), fasting and postprandial blood sugar tests were done in all patients of both groups. Gestational diabetes group patients had abnormal OGTT test reports and results were statistically significant (p <0.05) when interpreted along with FBS and PPBS. Among GDM patients, 2 patients advised for diet control and rest 28 were started on insulin therapy.

Table 2: Comparison of Homocysteine levels in both groups.

Homocysteine level	Normal pregnancy group		Pregnancy with GDM group	
	Primi	Multi	Primi	Multi
<15 µmol/l	10 (<5 mmol/l)	10 (<5 mmol/l)	7	6
>15 µmol/l	-	-	8	9
Mean value	3.8±0.95		16.30±6.09	
SD	95038		6.09711	
Statistical Inference	T= -9.024 Df=48 .000 <0.05 Significant			

Normal fasting homocysteine level in healthy individual is <15 mmol/l. Table 2 shows the comparison of Homocysteine levels in both groups. In this study normal pregnant women had the values of <5 micro mol/l. Among the 30 GDM patients 17 had elevated homocysteine level in which 8 were primi and 9 multigravidas. The mean value of homocysteine in control group was 3.8±0.95 and in gestational diabetes patients was 16.30±6.09 and its 'p' value was statistically significant. This study also evaluated the total cholesterol and triglyceride levels, 5 patients in control group and 18 patients of gestational diabetes patients had mild (>200 mg/dl) elevation of Total cholesterol. 12 patients of gestational diabetes patients had elevated TG level whereas all patients in control group had the normal triglyceride level. Total cholesterol and triglyceride level

is significantly (p=0.002) elevated in gestational diabetes patients. The mean value of total cholesterol in control group is 187.70±18.2 and in gestational diabetes patients is 211.50 ± 28.799. The mean value of triglyceride level in control and diabetes patients group were 113.30±16.10 and 140.20±22.15.

DISCUSSION

A systemic review showed a high prevalence of GDM in India (8.7%) and globally, the prevalence of hyperglycemia in pregnancy (GDM and manifest T2D in pregnancy) is estimated to be approx. 15%, for Europe, the prevalence is 12.6%.[2,3] GDM during pregnancy is associated with an up to 7-fold increase in the risk of manifest T2D compared with normoglycemic pregnancies.[4,5] GDM can adversely influence intrauterine development. Spontaneous abortions and major congenital anomalies may be induced in the first trimester. Excessive foetal growth, neonatal hypoglycaemia, jaundice, polycythaemia and stillbirth may be induced during the second and third trimesters.[6]

In 1991, Steegers Theunissen et al, suggested that maternal hyperhomocysteinemia (Hhcy) was a risk factor for neural tube defects.[7] Several studies also demonstrated that high tHcy is a risk factor of placenta-mediated diseases, such as preeclampsia, spontaneous abortion, placental abruption, and recurrent pregnancy loss.[8] Homocysteine is an intermediate which has an essential role at the junction of two major metabolic pathways in human physiology.

Hhcy can arise from nutritional deficiencies of folate, vitamin B6, vitamin B12 and defective metabolism of Plasma homocysteine.[9] Hhcy induces oxidative stress and antagonizes the vasodilator properties of NO by the formation of S-nitrosohomocysteine, thus leading to endothelial dysfunction and causes vascular hypertrophy and remodeling, impairs vascular properties and increases stiffness of arteries or arterioles.[10,11] Meigs et al, reported that increased serum Homocysteine is associated with increased insulin level in blood and suggested that it may cause cardiovascular disease risk when it is associated with insulin resistance.[12]

In our study the mean homocysteine level in control group is (3.8±0.95 µmol/L) is similar to that reported by Walker and associates in a Canadian population is 4.3 (95% confidence interval 3.5-5.3) at 20-28 weeks' gestation with normal glucose tolerance test and stated that Homocysteine levels were directly correlated with albumin levels, which decreased during pregnancy.[13]

The mean serum homocysteine concentration in women with gestational diabetes mellitus in our study was significantly higher than that in normal pregnant controls 16.30±6.09 µmol/L and 3.8±0.95 µmol/L respectively. A meta-analysis found that homocysteine levels were significantly elevated in women with GDM compared with those without GDM (weighted mean difference 0.77, 95% confidence interval 0.44-1.10).[14] Many other studies showed that Serum homocysteine was significantly higher in the group with GDM compared with nondiabetic women.[15,16]

On comparison of the serum homocysteine levels in gestational diabetes mellitus with normal pregnancy, in author study we found that there was hyperhomocysteinemia and results were statistically significant. (T= -9.024 Df=48 .000 <0.05). Guven group found higher homocysteine levels GDM patients compared to normal pregnant women, reported lower estimates (9.0±3.1 µmol/L and 7.4±1.6 µmol/L respectively) and statistically difference in homocysteine levels was observed between women with gestational diabetes and normal controls (P <0.01).[17]

The study carried out on 93 pregnant women evaluated for relationship between sHcy and glucose or insulin levels in normal pregnancy and with GDM, revealed significantly higher levels of Hcy in women with GDM, independently of other confounding variables, is significantly related to 2-hour OGTT plasma glucose, and seems unrelated to insulin resistance in these subjects.[18] In a prospective study, patients with gestational diabetes and women with abnormal screening test results (>135 mg/dL) but normal OGTT results have higher homocysteine levels than normal pregnant women.[19] Women with GDM had higher serum homo-cysteine levels than women with normal glucose tolerance (WMD 0.77, 95% CI 0.44-1.10). [13]

A multicentre European case–control study concluded that elevated levels of homocysteine are associated with increased risk of vascular risk even in the presence of desirable lipids and lipid subfractions.[20] Author study, total cholesterol and triglyceride level is significantly (p=0.002) elevated in gestational diabetes patients. GDM significantly alters serum cholesterol metabolism leading to dyslipidemia.

These findings co-relate with reports by Amraei and Azematidone in Pakistan who reported significant difference in total cholesterol levels between pregnancy complicated by GDM and normal pregnancy and also a meta-analysis shows that triglycerides are significantly elevated among women with GDM compared with women without insulin resistance and this finding persists across all three trimesters of pregnancy.[21,22]

Authors study had small sample size, lack the knowledge of homocysteine status of the patient before the diagnosis of the gestational diabetes mellitus. We failed to evaluate the role of other risk factors of gestational diabetes mellitus like insulin level, sensitivity of insulin, vitamin B12, B6 and folate level and the association between severity and outcome of maternal status and also fetal outcome with serum homocysteine levels.

CONCLUSION

In this study, authors found that patients with gestational diabetes mellitus have higher serum homocysteine levels in comparison with normal pregnant women. Hyperhomocysteinemia is found to be an independent risk factor for gestational diabetes mellitus patients. This increased level seems to be related to an elevated total cholesterol and triglyceride levels. Further investigations are needed to follow up for these patients in the postpartum period and later in their life for other vascular complications.

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