



Original Research Article

Evaluation of fasting plasma glucose, lipid profile and thyroid stimulating hormone as predictors of gestational diabetes mellitus

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ARTICLE INFO

Article history:

Received 20-07-2020

Accepted 24-08-2020

Available online 28-09-2020

Keywords:

First trimester

Fasting plasma glucose

Gestational diabetes mellitus

Lipid profile

TSH

ABSTRACT

Objective: To evaluate the usefulness of fasting plasma glucose, lipid profile, and thyroid-stimulating hormone (TSH) estimated at first trimester in predicting gestational diabetes mellitus.

Materials and Methods: A prospective study was done. Samples were collected after 12 hours of fasting from 250 women within the gestational age of 12 weeks and were analyzed for plasma glucose, lipid profile, and TSH in the fully automated analyzers EM 200 and Cobas e411 by enzymatic and electrochemiluminescence immunoassay respectively. Oral glucose tolerance test (OGTT) with 75 gm was performed in these subjects at 24–28 weeks of gestational age. Data was analyzed using SPSS 19.0. To analyze statistically significant differences in means of continuous variables between 2 groups, a student t-test was used. Multiple logistic regression analyses were performed to find the presence of association of these independent variables with GDM.

Results: Out of 250 pregnant women, 51 (25%) developed GDM, 149(75%) had normal glucose tolerance. GDM was found to have an association with fasting plasma glucose with (OR 2.846, 1.506- 5.362, P < 0.001), total cholesterol (OR 1.136, 1.072-1.120, P=0.04), triglycerides (OR 1.464, 1.361-1.565, P=0.003), low density cholesterol (LDL-C) -(OR 1.253, 1.173-1.338, P=0.009), and no association with TSH.

Conclusion: Estimation of fasting plasma glucose, lipid profile in the first trimester can be predictors of GDM, whereas TSH can not be a predictor of GDM.

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1. Introduction

Gestational diabetes mellitus (GDM), a common medical complication of pregnancy, is defined as “any degree of glucose intolerance with onset or first recognition during pregnancy”.^{1,2} GDM not only influences immediate maternal (preeclampsia, stillbirths, and need for cesarean section) and neonatal outcomes (hypoglycemia, respiratory distress) but also increases the risk of future type 2 diabetes in mother as well as the baby. The incidence of GDM is increasing globally. Commonly, GDM can be diagnosed by using the oral glucose tolerance test (OGTT) during 24-28 weeks of gestation.

However, maternal metabolic status at the early stage of pregnancy may affect maternal and perinatal outcomes.

Appropriate diet and medical interventions can reduce the incidence of GDM. Therefore, early detection of women at high risk of GDM is clinically important. It is estimated that about 4 million women are affected by GDM in India, at any given time point.³ Most researchers focused on identifying risk factors at the first trimester for GDM development, including family predisposition, increased maternal age, cultural background, high Body Mass Index (BMI), and history of fetal macrosomia. The efficiency of fasting plasma glucose (FPG) in predicting GDM is not universally agreed as different criteria are applied for the diagnosis and various gestational weeks or races are chosen.

One of the causal factors for perinatal morbidity and mortality could be the maternal atherogenic lipid profile early in pregnancy. During normal pregnancy, women show an increase in lipid levels, including levels of triglycerides (TG) and total cholesterol (TC) as gestational

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age progresses.⁴ Both TG and TC are taken up by the placenta and metabolized and transported to the fetus in various forms. However, high levels of maternal TC and/or TG are associated with preterm birth (PTB), preeclampsia, and pregnancy-induced hypertension (PIH).⁵

Likewise, the fetus is dependent on maternal thyroxine in early pregnancy. Maternal T₄ is transferred to the fetus throughout the entire pregnancy and is important for normal fetal brain development. After 15-18 weeks, the fetus controls most of its thyroidal secretion. Thyroid-stimulating hormone (TSH) is the most reliable measure of thyroid function during pregnancy. Subclinical hypothyroidism (elevated TSH with normal free T₄) is more common than overt hypothyroidism. Poor pregnancy outcomes seen are increased risk of preterm delivery, preeclampsia, etc. Untreated hypothyroidism leads to increased incidence of low-birth-weight infants, preeclampsia, placental abruption, pregnancy loss, and impaired fetal neurocognitive development. There is no clear evidence of first trimester estimated TSH association with GDM development in the previous studies.

Hence, this study aims to evaluate the association between first-trimester fasting plasma glucose level, lipid profile and TSH with the risk of developing GDM, so that if any association is found; then early steps can be taken to prevent the development of GDM and its complications.

2. Materials and Methods

This prospective study was conducted in the central laboratory, department of Biochemistry, KIMS & RF, Amalapuram. 250 pregnant women with a gestational age of ≤ 12 weeks who attended the OPD of Obstetrics and Gynaecology, KIMS&RF from June 2019 to January 2020 were included in the study.

Only subjects with singleton pregnancy without any history of pregestational diabetes, oral hypoglycaemic drugs usage, type 1 diabetes, known thyroid disease, chronic renal failure, diabetic nephropathy, with acute illness, with hepatic dysfunction and patients on treatment with drugs interfering with thyroid function (amiodarone, propranolol, corticosteroids, lithium, beta-blockers, iodides, alpha interferons) and those affecting the lipid profile were excluded from the study.

Prior permission was taken from the Institutional Ethics Committee of KIMS& RF, to conduct the study. All of the subjects provided their informed consent as approved by the ethics committee.

After 12 hours of fasting, under aseptic conditions, 10 ml of venous blood was collected in vacutainers. The blood was centrifuged and the plasma was collected and analyzed immediately in Erba 200 autoanalyzer.

Fasting glucose, total cholesterol, HDL (High-density lipoprotein), triglycerides were estimated by GOD- POD (Glucose oxidase-peroxidase) method, CHOD-POD

(cholesterol oxidase-peroxidase) method, CHOD-CHER (cholesterol oxidase- cholesterol esterase) method and GPO (Glycerol phosphate oxidase) method respectively. Plasma LDL-C (low-density lipoproteins) values were calculated using Friedewald's formula. TSH was estimated by electrochemiluminescence immunoassay in Cobas e411 analyser.

At 24-28 weeks of gestational age, OGTT with 75 gms of glucose was performed in these 250 women. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) consensus panel mean values of fasting (>92 mg/dl), 1 h (>180 mg/dl) and 2 h (>153 mg/dl) blood glucose of all pregnant females after intake of 75 gm oral glucose at 24-28 weeks of gestation was taken as a reference to confirm the diagnosis of GDM.

Data were analyzed using SPSS 19.0. Continuous variables were presented as mean \pm standard deviation. To analyze statistically significant differences in means of continuous variables between 2 groups, a student t-test was used. $P \leq 0.05$ was considered statistically significant. Multiple logistic regression analyses were performed to find the presence of association of these independent variables with GDM.

3. Results

Table 1:

Total Pregnant women included in the study	Gestational diabetes	Normal glucose tolerance
N = 250	N = 51 (25%)	N = 149 (75%)
Age (years) 30.57 \pm 4.13	32.29 \pm 4.42	30.15 \pm 4.33

Table 1 shows average age of the 250 women in the study was 30.57 ± 4.13 years. Women in GDM were significantly older than women in Normal glucose tolerance (NGT) group (32.29 ± 4.42) years vs. (30.15 ± 4.33) years, $P < 0.001$.

Table 2:

Continuous variable	P value	OR (95% CI)
Fasting plasma glucose	< 0.001	2.846 (1.506- 5.362)
Total Cholesterol	0.04	1.136 (1.072 - 1.120)
Triglycerides	0.004	1.469 (1.361 - 1.565)
LDL-C	0.008	1.253 (1.173 – 1.338)
TSH	0.217	1.871 (0.690 – 5.081)

Table 2, P values of continuous variables in GDM when compared with the Normal glucose tolerance group. The odds ratio with a 95% confidence interval is shown for the variables as obtained by logistic regression analysis.

4. Discussion

Out of 250 pregnant women who underwent OGTT at 24–28 weeks of gestational age, 51(25%) developed GDM, whereas 149(75%) had normal glucose tolerance. The average age of the 250 women in the study was 30.57 ± 4.13 years. Women in GDM were significantly older than women in normal glucose tolerance (NGT) group (32.29 ± 4.42) years vs. (30.15 ± 4.33) years, $P < 0.001$. These findings are similar to the previous studies which propose that as age advances, the incidence of GDM rises in pregnancy.

The fasting plasma levels in the GDM group, when compared to the NGT group, shows a statistically significant increase with a $P < 0.001$. The logistic regression analysis shows an association of fasting plasma glucose estimated in the first trimester with GDM with OR 2.846 (1.506–5.362). These findings agreed with the results of existing studies done by M Zhao, G H Li.⁶ Previous studies had showed that FPG could be used to predict risk for GDM in later pregnancy. In China, using a 2h 75-g OGTT and the IADPSG criteria, Min Hao et al. found FPG could be used in predicting suspicious GDM patients in the first trimester. An extensive study by Zhu et al. involving 17186 women using the IADPSG criteria, showed that the first prenatal visit FPG correlated strongly with GDM at 24–28 weeks gestation. This study also found association of FPG for predicting GDM when the IADPSG criteria was used.

Pregnancy is a diabetogenic state. Human placental lactogen is produced from the placenta at high levels during 24–28 weeks of pregnancy which contributes to increased insulin resistance in this period. Increased levels of estrogen, progesterone, and cortisol in pregnancy also contribute to hyperglycemia as they have anti – insulin-like action. Altered gluconeogenesis and lipolysis in pregnancy also contribute to hyperglycemia and the development of GDM. The etiology of GDM has been traditionally connected to dysregulation of placental hormones favouring the discharge or effect of those that interfere with insulin sensitivity.⁷ The unbalanced hormone secretion and/or β -cell injury, some other potential risk factors have been suggested for GDM. Furthermore, other studies have concluded that GDM may be mainly originated from β -cell injury.

The results of the present study revealed that serum levels of TC, TG, and LDL-C all increased significantly in the GDM group when compared to NGT group with a $P < 0.04$, 0.004, 0.008 respectively. The logistic regression analysis shows an association of total cholesterol, triglycerides and LDL-C estimated in the first trimester with GDM with OR 1.136 (1.072 - 1.120), 1.469 (1.361 - 1.565), 1.253 (1.173 – 1.338) respectively.

The changes in maternal lipid concentrations during pregnancy observed in this study were similar to those reported in previous studies that showed that blood lipid concentrations increased during pregnancy, with TG levels changing the most.^{8,9} Changes in serum lipid levels

during pregnancy are thought to be affected by hormonal changes, including increases in serum levels of estrogen and progesterone.^{10–12}

Adipose tissue and placenta can produce a similar pattern of cytokines, which explains the fact that these women are at higher risk of GDM.

The β -cell number can decrease by 41% in GDM mothers,¹³ potentially due to the delivery of “toxic” adipokines.¹⁴ Indeed, maternal obesity and GDM may be associated with a state of chronic, low-grade inflammation by which offspring are programmed to develop adult disorders.¹⁵ Also, overproduction of ketone bodies i.e., α -hydroxybutyrate (AHBA), typical in obesity, paralleled the impairment of insulin secretion during gestation and GDM.¹⁶

The current study confirmed a trend towards an increasing incidence of GDM with increasing levels of TC, TG, and LDL-C in early pregnancy. These findings agreed with the results of existing studies. Vrijkotte TG et al. found that every unit increase in TG levels during early gestation was linearly associated with an increased risk of hyperglycemia in pregnancy, preeclampsia, and preterm delivery, suggesting that lifestyle programs should be conducted in women of reproductive age with a focus on lowering triglyceride levels.

Moreover, an increase in TC and LDL-C levels during pregnancy is also considered a risk factor for GDM, preterm delivery, and Pre eclampsia.^{17–19} Disturbances in maternal lipid metabolism have been shown to increase the risk of adverse pregnancy outcomes, including gestational diabetes mellitus (GDM), pre-eclampsia (PE), preterm birth, and fetal growth disorders.²⁰

The first trimester TSH levels in the GDM group when compared to the NGT group was found to have no statistical significance with a $P > 0.05$. It is found in this study that there is no association of TSH measured in the first trimester with GDM.

These results are similar to the previous study done by Ping li, et al²¹ which suggested that maternal subclinical hypothyroidism in the first trimester was not related to GDM, regardless of the thyroid peroxidase antibody (TPOAb) status or the TSH levels.

5. Conclusion

The present study-“Evaluation of fasting plasma glucose, lipid profile and thyroid-stimulating hormone as predictors of gestational diabetes mellitus” concludes that there is an association of fasting plasma glucose, lipid profile with Gestational diabetes mellitus. There is no association of TSH estimated in the first trimester with Gestational diabetes mellitus.

Thus, fasting plasma glucose and lipid profile especially triglycerides can be used as predictive markers of Gestational diabetes mellitus. The study cannot include

certain other confounding factors as BMI (Body mass index), etc, and the validation of result is required by doing the study with a larger sample size.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Saumya V. Evaluation of fasting plasma glucose, lipid profile and thyroid stimulating hormone as predictors of gestational diabetes mellitus. *Int J Clin Biochem Res* 2020;7(3):357-360.