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Using 75 g OGTT in Prediction for Macrosomia in Gestational Diabetes Mellitus

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Introduction

Gestational Diabetes mellitus (GDM) is defined as carbohydrate intolerance with different degrees of severity which occurs or is recognized for the first time during pregnancy. Fetal birth weight above the 90th percentile for gestational week and newborns weight equal or higher than 4000 g is defined as macrosomia [1]. About 15-45% of babies born from mothers with GDM can have macrosomia, which is 3-fold higher in comparison to normoglycemic controls (12%). Macrosomic infants from mothers with GDM are related to risk of developing overweight, obesity in adulthood, and type 2 diabetes mellitus and cardiovascular diseases later in life. Several studies showed that epigenetic alterations of different genes of the fetuses of a GDM mother in utero could result in transgenerational transmission of GDM and type 2 diabetes mellitus [1]. Thus, hyperglycemia begets hyperglycemia.

There is no doubt that maternal hyperglycemia plays a very important role in fetal overgrowth [1,2]. The first hour after beginning of the meal is associated as best predictor of subsequent macrosomia [2]. Unlike maternal hyperglycemia, obesity is the strongest and independent predictor for fetal macrosomia [3,4]. Maternal pre-pregnancy body mass index (BMI) [1], pregnancy weight gain [2], maternal height, maternal age at delivery, hypertension and cigarette smoking have a significant impact.

The predictive ability of the glucose levels from the 2-h 75-g OGTT in terms of pregnancy outcomes has been investigated little until the HAPO study [5]. Thus, the objective of the mini report is to evaluate the association between glucose levels of 75-g OGTT and perinatal outcomes, in 118 pregnant women who were prospectively screened for GDM between 24 and 28 weeks of pregnancy [6].

Subjects and Methods

This prospective study consecutively enrolled 118 adult women attending Clinic of Endocrinology. All women underwent standardized 2 h 75 g oral glucose tolerance test (OGTT) between 24th and 28th gestational weeks and were followed until delivery. New ADA criteria were used [6].

Results

The primary outcome was macrosomia (BW>4000 g), gestational week of delivery and cesarean delivery. Twenty one (30.4%) of the neonate in the GDM group were LGA (adjusted weight at or above 90th percentile) and this significant differs from the control group (P<0.01). We found significant correlations between LGA newborns from GDM pregnancies with fasting plasma glucose (r=0.46, p<0.05)

(Figure 1), and 1 h OGTT plasma glucose levels (r=0.30, p<0.05) (Figure 2). We also noted 2 significant correlations between FPG with BMI before pregnancy (r=0.47, p<0.01), BMI before delivery (r=0.47, p<0.01), and HbA1c (r=0.25, p<0.05 (Figure 3).

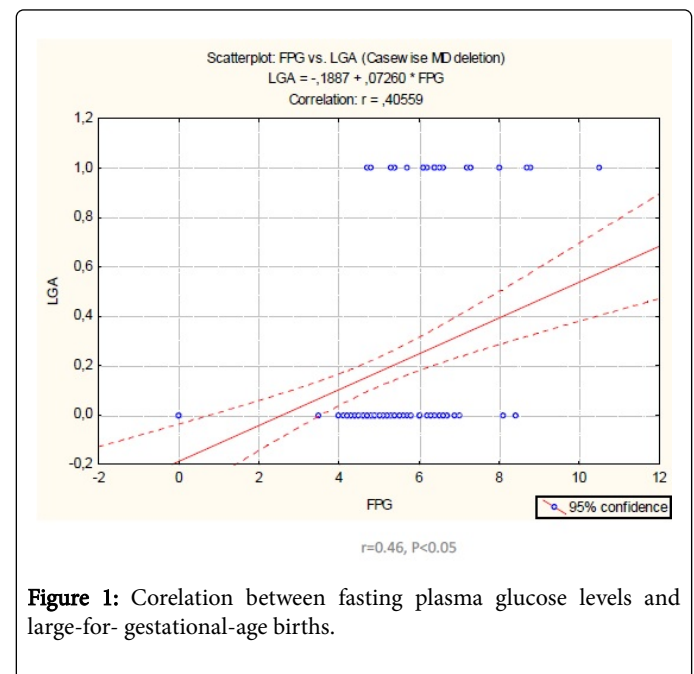


Figure 1: Correlation between fasting plasma glucose levels and large-for-gestational-age births.

In order to evaluate fasting, 1 h and 2 h OGTT glucose levels for the prediction of LGA, we compared the areas under the receiver operator characteristic curve (AUC) of the ROC curves. Figure 4 shows that, for LGA newborns from GDM pregnancies, fasting AUC was 0.782 (0.685-0.861), for 1 h OGTT was 0.719 (0.607-0.815), and for 2-h OGTT was 0.51 (0.392-0.626). Fasting glucose levels and 1 h OGTT glucose levels show statistically significant predictability for LGA (p<0.05) than 2 h OGTT glucose levels.

Discussion

The results of the study confirmed that gestational diabetes pregnancies were complicated with LGA newborns in contrast to normal pregnancies. We also showed that fasting plasma glucose and 1 h post load glucose levels from 75 g OGTT were strongest predictor for LGA newborns of mothers with GDM. Our results accent the role of maternal FPG upon the development of macrosomia in the newborn.

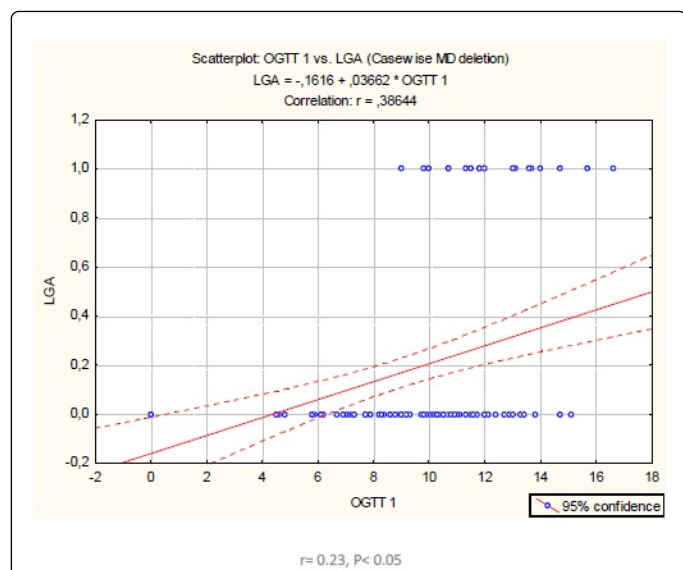


Figure 2: Correlation between 1 h OGTT plasma glucose levels and large-for gestational-age births.

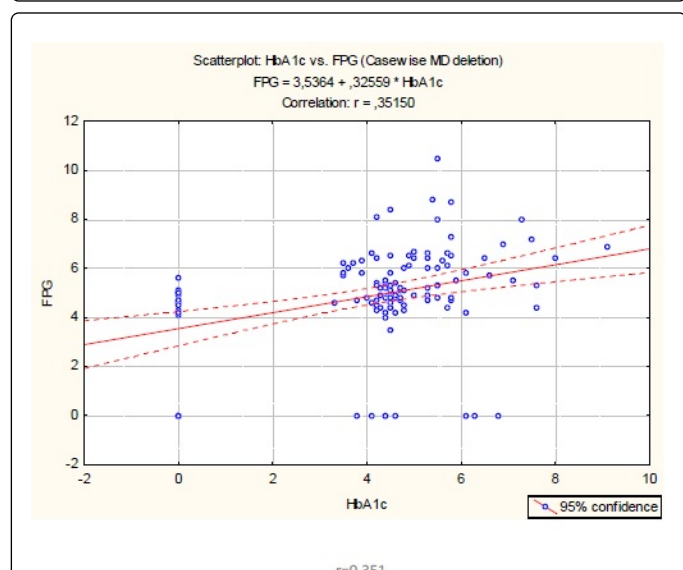


Figure 3: Correlation between HbA1c and fasting plasma glucose levels.

Data from this study confirmed earlier work linking mild glucose intolerance with adverse perinatal outcomes. Actually, in the HAPO (Hyperglycemia and Adverse Pregnancy Outcome) study the authors presented a strong association between increasing levels of fasting, 1 h and 2 h plasma glucose obtained on OGTT with LGA and cord-blood C-peptide levels, but a weaker association between glucose levels and primary cesarean delivery and neonate hypoglycemia. In conclusion, if more than one glucose level is exceeded, the chances for delivering LGA newborns are higher [5]. According to our results, FPG of 5.8 mmol/l and 1 h glucose values of 11.1 mmol/l (derived from the 75 g OGTT) strongly predict LGA, and indicate direct association between glucose levels and macrosomia [6]. Furthermore, Aktun HL et al. in

their study found that a fasting plasma glucose >105 mg/dl (5.8 mmol/L) might be used to identify high-risk pregnant women requiring insulin treatment, and FPG and HbA1c levels were found to be predictors for insulin treatment at the time of diagnosis [7]. So, at the time of diagnosis tight glucose control in these target women and frequent fetal monitoring may be necessary to avoid macrosomic babies.

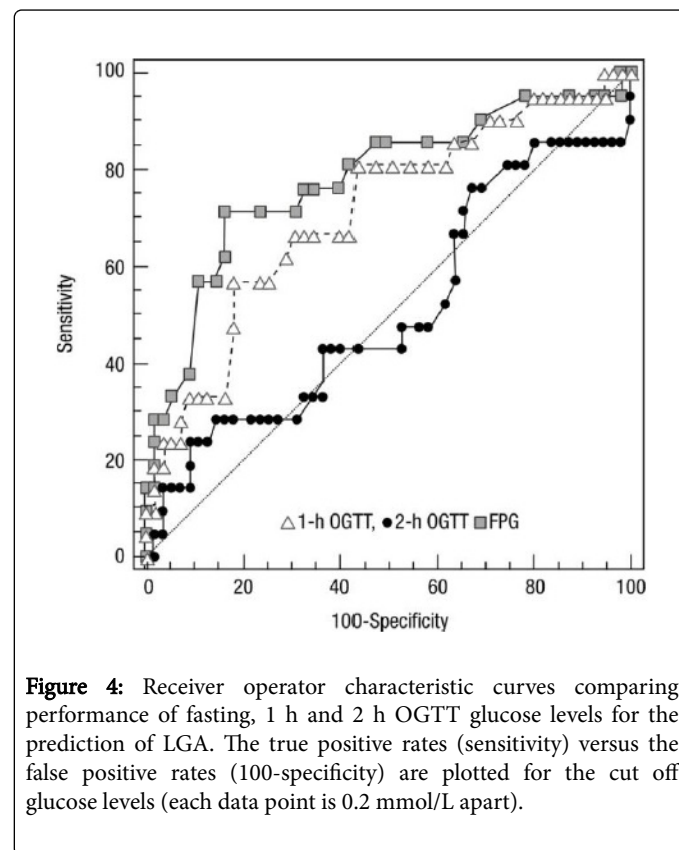


Figure 4: Receiver operator characteristic curves comparing performance of fasting, 1 h and 2 h OGTT glucose levels for the prediction of LGA. The true positive rates (sensitivity) versus the false positive rates (100-specificity) are plotted for the cut off glucose levels (each data point is 0.2 mmol/L apart).

Our finding that fasting plasma glucose values were the strongest predictor for LGA, may point out the difference in pathophysiology between high fasting plasma glucose and post-load glucose intolerance. Fasting plasma glucose reflects altered basal insulin secretion and impaired suppression of hepatic glucose production. Post-load glucose intolerance reflects altered first-phase of insulin secretion, peripheral tissues insensitivity and diminished ability of insulin to suppress hepatic glucose production. This association between FPG and LGA suggest that other maternal factors contributing to high FPG may contribute to developing macrosomia, such as BMI. We found significant correlations between FPG and pre-pregnancy BMI and FPG with pre-delivery BMI. Therefore, adverse perinatal outcomes can be found potentially in GDM patients with higher BMI and abnormal FPG. Moreover, Park et al. proposed very practical and efficient screening tool as predictor of adverse perinatal outcomes using FPG and prepregnancy BMI [8]. The factors most consistently predictive of fetal weight are maternal weight followed by maternal weight gain. In our study regression analysis did not show that pre-pregnancy BMI and BMI before delivery were independent predictors of macrosomia. Our results are not in line with those of Bernthrop et al., who found that maternal BMI had a greater impact on the prediction of LGA birth than 2 h glucose level of the OGTT [9].

The degree to which levels of maternal hyperglycemia contribute to macrosomia has been the subjects of much debate. Since 1986 year,

many authors found that women with abnormal glucose screens had a higher rate of macrosomia compared to women with normal glucose screens [10-12]. In addition, other 3 studies revealed that the risks of macrosomia increased with higher 50 g CGT values, as denoted in the paper of Kemal Akpak, who defines 50 g CGT value of 140 mg/dl (7.8 mmol/l) as cut of value for women with risk factors, and glucose of 159 mg/dl (8.8 mmol/l) as cut of value for those patients with no risk factors. The same study points out that first hour glucose values of 180 mg/dl (10 mmol/l) or higher are associated with poor perinatal and fetal outcomes [13]. The literature data offer possibilities to define more precise cut-off glycemic values that might indicate higher risk of adverse perinatal outcomes [14-16].

The macrosomia rate was more dependent on the presence of fasting hyperglycemia, post-load hyperglycemia, overweight and obesity in GDM pregnancy. This analysis does not address glycemic control, but rather prognostic implications of results of the 2 h OGTT.

Conclusion

We can use 75-g OGTT in the prediction of neonatal macrosomia and maternal outcome. Maternal fasting and 1 h glucose values from OGTT correlate closely with the birth weight and are the strongest predictors for macrosomia.

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