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Predictive Parameters of Gestational Diabetes Mellitus

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A B S T R A C T

Gestational diabetes mellitus is a carbohydrate intolerance recognized in pregnancy. The objective of this study was to determine the prevalence of gestational diabetes mellitus (GDM) of all deliveries at the University Hospital Rijeka, Croatia (34 997 deliveries over 10-year period) using 2-hour 75 g oral glucose tolerant test and to evaluate the impact of GDM on neonatal outcomes and mother's health. Gestational diabetes was diagnosed in 55 of 128 pregnant women with suspected glucose intolerance. Logistic regression analysis was used to examine the relationship between fasting plasma glucose, age, family history, body mass index, maternal weight gain, neonatal weight, neonatal head diameter and Apgar score in the gestational diabetes group and in the non-diabetes group. The results indicate that fasting plasma glucose greater than 7.0 mmol/L and maternal overweight are strong predictors for GDM and macrosomia. There was no difference in the mode of delivery, and vitality and metabolic complications among the infants of all analyzed mothers. We concluded that to prevent GDM as well as to reduce the rate of macrosomic infants good glycemic control should be initiated as soon as possible. The 2-hour 75 g OGTT is worth enough to evaluate GDM. Women should be counseled and encouraged to lose weight before or at the beginning of the conception period.

Key words: *gestational diabetes mellitus, fasting plasma glucose, oral glucose tolerance test*

Introduction

Gestational diabetes mellitus (GDM) is a carbohydrate intolerance recognized in pregnancy[1–3]. This definition also includes previously undiagnosed diabetes or impaired glucose tolerance (IGT). GDM is induced by maternal insulin resistance and usually develops in the second trimester of pregnancy[4,5]. The impaired insulin secretion and insulin in-sensitivity also play an important role in the GDM pathogenesis[6,7]. The development of GDM is connected with serious implications on pregnancy, the future health of the mother, and may also affect the health of the fetus and the child[8–11].

There is no firm consensus regarding the diagnostic criteria for GDM[12–14]. Of the several criteria employed to diagnose GDM in Europe, most have not been equally applied in pregnancy. The screening technique typically used in the United States is an l-hour 50 g oral glucose challenge test (GCT), with a subsequent 3-hour l00 g glucose tolerance test (OGTT) for women whose GCT is positive[15]. In the attempt to standardize the diagnosis of GDM, the WHO has proposed using a 2-hour 75 g OGTT[6]. In GDM 1-hour glucose levels do not differ after 75 g or 100 g loads or after glucose measurement in capillary or venous plasma[16]. Some authors suggest a breakfast glucose test as useful in identifying a high-risk population in which clinic follow-up may be used safely[17].

This study was conducted to determine the prevalence of GDM among women receiving regular prenatal care at the Clinic of Obstetrics and Gynecology. We were also interested in identifying the risk factors for GDM development (age, maternal weight and weight gain, body mass index, family history) and to determinate their consequences on neonatal birth weigh and their relationship with the newborn's and mother's outcomes.

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Subjects and Methods

Over the period of 10 years we have analyzed 140 pregnant women with hyperglycemia. Patients with fasting plasma glucose (FPG) higher than 7.0 mmol/L (venous plasma) have been identified as hyperglycemic patients. The examination started with a family history of diabetes mellitus or hypertension. The measurement lasted 2 days. All pregnant women with hyperglycemia were submitted to 2-hour 75 g OGTT from full venous blood. Values of the test were analyzed using the WHO criteria. All data analyzed were from women between 24–28 weeks of pregnancy. The weight of the pregnant women was based on body mass index (BMI) before pregnancy and weight gain during pregnancy. The routine biochemical and hematological blood analysis were performed. Tocography and ultrasonic examination were performed in all pregnant women. The condition of newborn babies was estimated on the basis of birth weight, neonatal head diameter and Apgar score at one and five minutes.

All statistical analysis was done using the SAS System package on Windows platform. Univariate analysis was performed comparing the difference in all the variables between the non-diabetes and gestational diabetes group. The significance of difference was assessed by Wilcox on rank-sum test for the continuous variables and by t-test for the categorical variables. Logistic regression was performed to find possible predictors of gestational diabetes group. Probabilities of less than 0.05 were accepted as significant.

Results

Of the 140 pregnant women examined for the diagnosis diabetes, 12 were on intense insulin therapy (8.6%), and 128 had suspected glucose intolerance (91.4%). In the group with suspected glucose intolerance a 2-hour 75 g OGTT was carried out. Glucose intolerance was confirmed in 55 (42.9%) while 73 of 128 women (57.1%) had normal OGTT values.

The features of healthy and GDM patients were collected (Table 1.) and the following variables were compared between the two groups: fasting plasma glucose – first day (FPG1), fasting plasma glucose – second day (FPG2), age (A), family history (FH), body mass index (BMI), maternal weight gain (MW), neonatal weight

TABLE 1
GENERAL CHARACTERISTICS OF THE PATIENTS: NON DIABETES VERSUS GESTATIONAL DIABETES

	Deliveries with gestational diabetes (N=55)	Healthy deliveries (N=73)	p
A	32.20±5.87	29.99±5.56	0.0475
MW	15.86±3.49	12.78±5.33	< 0.001
BMI	29.29±5.16	24.77±2.68	< 0.001
FPG1	6.39±0.64	6.00±0.28	< 0.001
FPG2	6.49±0.63	6.16±0.44	0.0037
NHD	35.44±1.29	34.59±1.44	0.001
AS1	8.00±1.58	7.90±1.77	0.7278
AS5	8.95±1.31	8.67±1.31	0.1395
NW	4178.00±549.01	3563.70±513.98	< 0.001
	N / %	N / %	
FH neg.	40 / 72,73	58 / 79.45	0.374
FH pos.	15 / 27.27	15 / 20.55	

A – age, MW – maternal weight gain, BMI – body mass index, FPG1 – fasting plasma glucose – first day, FPG2 – fasting plasma glucose – second day, NHD – neonatal head diameter, AS1 – apgar score after one minute, AS5 – apgar score after five minutes, NW – neonatal weight, FH – family history

TABLE 2
SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUES, NEGATIVE PREDICTIVE VALUES AND DIAGNOSTIC EFFICIENCY ACCORDING TO TRESHOLDS FOR THE MODELS IN THE PREDICTION OF GESTATIONAL DIABETES MELLITUS

Model	Treshold	Sensitivity (%)	Specificity (%)	False positive (%)	False negative (%)	Diagnostic efficiency (%)
Z1	–0.31008	87.27	83.56	20.00	10.29	85.16
Z2	–0.21428	81.82	84.93	19.64	13.89	83.59
Z3	–0.21922	81.82	84.93	19.64	13.89	83.59

(NW), neonatal head diameter (NHD), Apgar score after the first minute (AS1) and Apgar score after the fifth minute (AS5). Univariate analysis showed significant difference in mean values of the two groups, for all the variables except for AS1 and AS5. The patients from the gestational diabetes group were slightly older than the non-diabetes group (mean of 32.2 years in gestational group vs. 30.0 years in non-diabetes group, p=0.0475). Both FPG variables, as well as NHD and all three obesity related variables (NW, MW and BMI), were on average significantly higher in the gestational diabetes group.

Logistic regression was performed to identify which variables in combination predicted GDM. We included all potential predictive variables in the model and, using the backward elimination stepwise approach, eliminated one by one the variables that did not significantly contribute to the prediction of gestational diabetes. The variables were FPG1, FPG2, A, FH, BMI, NW, MW, NHD, AS1 and AS5. After the elimination of the no significant variables, a combination of four variables was found to be a significant predictor in the model: FPG1, BMI, AS5 and NW. The resulting model for the prediction of gestational diabetes mellitus was: Z1= –32.35 + 1.77 x FPG1 + 0.31 x BMI + 0.47 x AS5 + 0.0023 x NW. Further, we constructed an additional model in which we included all the resulting variables from the previous model, as well as their interactions (FPG1 x AS5, FPG1 x NW, FPG1 x BMI, AS5 x NW, AS5 x BMI, and NW x BMI). After the elimination of no significant variables, just two of all the variables remained in the model as significant predictors of gestational diabetes: FPG1 x BMI and FPG1 x NW. The resulting model was: Z2 = –15.40 + 0.05 x FPG1 x BMI + 0.0003 x FPG1 x NW

Comparing the two models we observed that in the second model (Z2) there was no ASB5 variable, so we additionally tested the new model with variables FPG1, BMI and NW. The resulting model was: Z3 = –28.34 + 1.96 x FPG1 + 0.31 x BMI + 0.002 x NW

The sensitivity, specificity and diagnostic accuracy of these three models were also analyzed (Table 2.) Using the receiver-operating curve (ROC) for all the models we determined the threshold values maximizing the sensitivity and specificity of each model.

Discussion

According to the records of the Clinic of Gynecology and Obstetrics at the Clinical Hospital Center Rijeka, only 0.034% pregnant women have type 1 diabetes mellitus. The incidence of type 1 diabetes mellitus in our region is 2.2% of the population[18]. The incidence of fasting hyperglycemia among the total number of deliveries is also small (0.36%, namely 128 cases). The threshold of our fasting glycemic values is probably the reason for the true »pathological hyperglycemia«. Nevertheless, the threshold values for hyperglycemia estimation in pregnancy are not small, and they are more useful in identification among the overall population in which further investigation may be necessary[13].

We have been using 2-hour 75 g OGTT as a second step to diagnose GDM for many years now. Usually the prevalence of GDM reported in the literature is from 0.15 to 15%[6,19,20]. In a fasting hyperglycemia group we found positive OGTT in 43% (55 of the 128 pregnant women), which is 0.16% of total number of deliveries. As we measured FPG and obtained higher limit values with OGTT as well, we considered that the FPG was sufficient in evaluating GDM. Lowering the cut point of glycemia we can increase sensitivity but decrease specificity. Decreasing the limit values of OGTT could even result in over diagnosis of GDM. Although it is open to discussion which of the criteria are better to use – the WHO criteria or the GDM diagnose criteria recommended by the American Diabetes Association, a uniformly standardized test could be more useful in comparing the results of different GDM studies.

We found that pregnant women with diabetes mellitus and GDM were overweight during pregnancy, and some, before pregnancy as well. The maternal glucose level increase in a 2-hour 75 g OGTT could be largely explained by an increasing BMI[21]. Overweight is probably the reason for induction of GDM and consequently maternal insulin resistance or impaired insulin secretion or insulin sensitivity[5,7,22]. The opinion that insulin secretion is affected by gene mutation is not confirmed[23]. Even moderate overweight status is a significant risk factor for obstetrical and fetal complication[24,25]. The authors confirm that macrosomia is more frequent in pregnant overweight women[26]. To prevent some of the complications it is necessary to decrease BMI, even before pregnancy as well as during pregnancy, both with adequate nutrition and exercise[27,28].

Our opinion is that BMI is more predictive of macrosomia than weight gain. However, weight gain between pre-pregnancy and postpartum as well as insulin resistance in late pregnancy can predict abnormalities of glucose tolerance soon after delivery[29].

We did not find any congenital malformation in newborns and it confirms the Jenssen et al. statement that there is a weak association between congenital malformations and GDM[30]. According to the Apgar score there was no difference between newborn babies in our study, which is in accordance with some other findings[31,32].

Our results indicate that overweight before and during pregnancy together with a FPG greater than 7.0 mmol/L in the third trimester of pregnancy are strong predictors for GDM, and to GDM-related complications. The 2-hour 75 g OGTT is worth enough to confirm GDM. The reduction in weight before and during pregnancy by adequate nutrition and physical activity, as well as the early detection and appropriate treatment of GDM are representing crucial measures in appropriate treatment of pregnancy in women at high risk for GDM development.

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PREDIKTIVNI BILJEZI GESTACIJSKOG DIJABETESA

SAŽETAK

Gestacijski dijabetes melitus (GDM) je intolerancija glukoze u trudnoći. Cilj studije je bio odrediti prevalenciju GDM u ukupnom broju poroda Kliničkog bolničkog centra Rijeka, Hrvatska, tijekom desetogodišnjeg razdoblja (ukupno 34 997 poroda) korištenjem dvosatnog testa opterećenja sa 75 g glukoze i procijeniti utjecaj GDM na zdravstveni status čeda i majke. GDM je potvrđen u 55 od 128 trudnica kod kojih je postavljena sumnja na poremećaj metabolizma glukoze. Logističkom regresijskom analizom je ispitan odnos razina glukoze natašte, obiteljske opterećenosti dijabetesom, indeksa tjelesne mase, majčinog dobitka na težini tijekom trudnoće, porođajne težine čeda, njegovog opsega glave i Apgar zbira između skupina sa i bez GDM. Utvrđeno je kako su razine glukoze natašte veće od 7,0 mmol/L i pretjerana uhranjenost majke snažni prediktori GDM i makrosomije. Usporedba skupina po prisutnosti GDM-a isključila je postojanje značajnih razlika prema vrsti porođaja, te vitalnosti i metaboličkim komplikacijama novorođenčadi. Pravodobno otkrivanje sklonosti poremećaju metabolizma glukoze u trudnoći i poduzimanje mjera za prikladnu regulaciju glikemije, presudni su za sprečavanje nastanka GDM i smanjenje učestalosti novorođenačke makrosomije. Za postizanje navedenog cilja, od presudnog je značaja sustavno provođenje mjera edukacije žena i omogućavanje stručne potpore u prekoncepcijskoj regulaciji tjelesne težine.