

## CORRELATIONS BETWEEN THE VALUES OF MATERNAL GLYCEMIA FROM THE LAST TRIMESTER OF PREGNANCY AND FETAL BIRTH WEIGHT

Monica Veres<sup>✉</sup>, Aurel Babeş, Szidonia Lacziko

University of Oradea, Faculty of Medicine and Pharmacy

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### Abstract

**Background and aims:** Gestational diabetes represents a form of diabetes diagnosed during pregnancy that is not clearly overt diabetes. In the last trimester of gestation the growth of fetoplacental unit takes place, thus maternal hyperglycemia will determine an increased transplacental passage, hyperinsulinemia and fetal macrosomia. The aim of our study was that of analyzing the effect of maternal glycemia from the last trimester of pregnancy over fetal weight. **Material and method:** We run an observational study on a group of 46 pregnant women taken into evidence from the first trimester of pregnancy, separated in two groups according to blood glucose determined in the third trimester (before birth): group I normoglycemic and group II with hyperglycemia (>92mg/dl). **Results:** The mean value of third trimester glycemia for the entire group was of  $87.13 \pm 22.03$ . The mean value of the glycemia determined in the third trimester of pregnancy was higher in the second group (109.17 mg/dl) in comparison to the first group (74.,21 mg/dl). The ROC curve for third trimester glycemia as fetal macrosomia appreciation test has an AUC of 0.517. **Conclusions:** Glycemia determined in the last trimester of pregnancy cannot be used alone as the predictive factor for fetal macrosomia.

**key words:** gestational diabetes, hyperglycemia, macrosomia.

### Background and aims

Gestational diabetes represents a form of diabetes diagnosed during pregnancy that is not clearly overt diabetes and represents an increased risk factor for maternal and fetal perinatal complications. Maternal hyperglycemia affects the maternal placental blood flow leading to fetal distress, preeclampsia and/or fetal hypotrophy. Vascular modifications induced by hyperglycemia including thinning of the

basement membrane, endothelial cell proliferation and modifications of peri-vascular space by collagen deposition, proteoglycans and glycosaminoglycans can affect even placental and uterine vessels, affecting the maternal-fetal exchange process. On the other hand maternal hyperglycemia determines an increased transplacental passage of glucose, hyperinsulinemia and fetal macrosomia.

The aim of our study was to evaluate the effect of third trimester hyperglycemia on fetal

✉ 6 Aleea Călinului Street, Oradea, Postal Code 410234, Romania; Phone: 0359425192;  
corresponding author e-mail: moni\_veres76@yahoo.com

birth weight, macrosomia risk and perinatal complications.

### **Material and method**

We have run an observational study on a group of 65 pregnant women taken into evidence from the first trimester of pregnancy in Oradea Clinical Hospital for Obstetrics and Gynecology between January 2009 and June 2011. From the 65 women included in the study, the monitoring of glycemic status during the third trimester (before giving birth) was done only on 46 future mothers, these women representing our study's subjects. For each woman was created a file in which we registered: age, background, height and weight, information used for calculating body mass index (BMI), gestational age when registered, personal physiological and pathological history, along with obstetric history, blood pressure, pill and intoxicants consumption. In the personal file was also registered the presence of risk factors which may cause gestational diabetes, as it follows: family history of hyperglycemia, obesity, parity, antecedents of previous macrosomic fetus deliveries and the presence of glycosuria when taken under observation.

*Inclusion criteria* were: pregnant women with monofetal pregnancy and with physiological evolution of the pregnancy, which known first and third trimester glycemic value.

*The exclusion criteria* were: under age pregnant women (under 18), maternal chronic diseases, pathology associated to the pregnancy, twin pregnancy, conception after ovarian stimulation treatment or in vitro fertilization, chronic consumption of pills or intoxicants.

Plasma glucose levels were obtained from maternal venous blood in the first and third trimester of pregnancy (the period just before giving birth).

For each pregnant woman the pregnancy evolution was monitored by periodic obstetrical

examinations, which included 2D scanning and Doppler ultrasound. The first ultrasound examination was done in the case of all future mothers when taken into evidence, in the first trimester of pregnancy, to determine gestation age. If there has been noted a gap bigger than 5 days between pregnancy age calculated on LMP (Last Menstrual Period) basis and that estimated by the ultrasound within 6 – 13 weeks, pregnancy age was rectified on the basis of ultrasound parameters (CRL) (Crown- Rump Length). Doppler ultrasound examination consisted in the determination of velocimetric indices on umbilical artery and on middle cerebral artery, but also in determining uterine circulation, starting with week 20 – 24 of gestation, and during other prenatal consultations. Fetal growth was monitored by running fetal biometry and ultrasound estimation of fetal weight. The appearance of possible perinatal complications (preeclampsia, fetal hypotrophy/macrosomia, chronic or acute fetal distress during labour, respiratory distress syndrome) was registered.

We separated the pregnant women in 2 groups: group I with normal glycemia values (including 29 subjects) and group II, with hyperglycemia during the third trimester of pregnancy (>92 mg/dl), including 17 subjects. According to the International Association of Diabetes and Pregnancy Study Groups (IADPSG), the cut-off value of maternal fasting hyperglycemia was set at 92 mg/dl [1].

### *Statistic analysis*

Quantitative data are expressed as average  $\pm$  standard deviation. The statistic comparison of the data was done using the Student *t* test to compare the average values of the different characteristics of the groups and Pearson correlation test to compare two characteristics of a group. The P value was considered significant at  $\alpha = 0.05$ . The diagnostic relevance of third

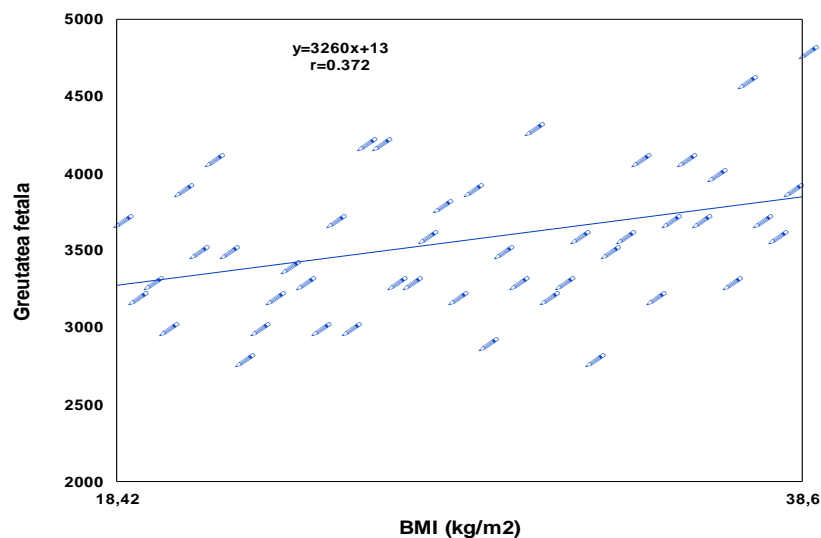
trimester glucose values for fetal birth weight prediction was investigated with the help of the area under the ROC curve (AUC). The confidence interval (95%), diagnostic level, sensitivity and specificity were determined. For statistical analysis we used the SPSS 19 and MedCalc 12.2.1 software.

## Results

The demographic and constitutional maternal parameters as well as predisposing factors for gestational diabetes are represented in [Table 1](#).

**Table 1.** Demographic parameters and predisposing factors for gestational diabetes

Social- demographic and constitutional parameters	WHOLE GROUP (N= 46)	GROUP I with normal glucose values (N= 29)	GROUP II with hyperglycemia in the third trimester of pregnancy (N= 17)	p
AGE (years)	28.02± 4.86 Min: 20 Max:43	27.89±4.39 Min: 21 Max:43	28.23±5.71 Min: 20 Max:41	0.06
BMI (kg/m <sup>2</sup> )	25.45±3.71 Min: 19.50 Max: 38.60	25.33±2.81 Min: 20.70 Max: 33.70	25.65±4.98 Min: 19.50 Max: 38.60	0.06
PARITY	1.58±1.12 Min: 1 Max: 7	1.69±1.25 Min: 1 Max: 7	1.41±0.87 Min: 1 Max: 4	0.1
RISK FACTORS	2 macrosomia 2 multiparous 1 father with diabetes	2 macrosomia 1 multiparous 1 father with diabetes	1 multiparous	



**Figure 1.** The correlation between BMI when taken into evidence and fetal birth weight

As shown in [Figure 1](#), we determined a linear positive correlation between maternal BMI when taken into evidence and fetal birth weight ( $r=0.372$ ,  $p<0.01$ ).

First and third trimester glycemia values are given in [Table 2](#). As shown, the values of third

trimester glycemia ranged between 49.50 mg/dL and 163 mg/dL, with a mean blood glucose value of  $87.13\pm 22.03$  mg/dL.

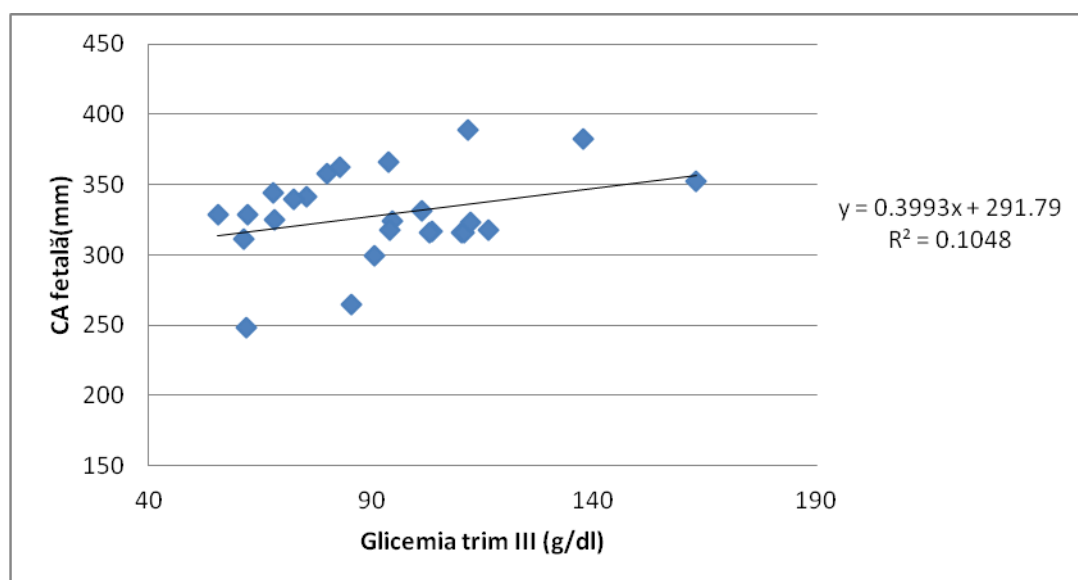
Ultrasound parameters as well as Doppler velocimetry indices measured in the third trimester of pregnancy are given in [Table 3](#).

**Table 2.** Fasting blood glucose recorded during the first and third trimester of pregnancy.

BIOLOGICAL PARAMETERES	WHOLE GROUP (N= 46)	GROUP I with normal glucose values (N= 29)	GROUP II with hyperglycemia in the third trimester of pregnancy (N= 17)	p
GLYCEMIA IN THE FIRST TRIMESTER (mg/dL)	60.87±42.96 Min: 65 Max: 140.2	55.24±41.02 Min: 65.9 Max: 116.3	70.50±44.11 Min: 65 Max: 140.2	0.2
GLYCEMIA IN THE THIRD TRIMESTER (mg/dL)	87.13±22.03 Min: 49.5 Max: 163	74.21±11.46 Min: 49.5 Max: 91.5	109.17±17.81 Min: 92.6 Max: 163	0.1

**Table 3.** Ultrasound paramaters and Doppler velocimetry indices.

Ultrasound paramaters and Doppler velocimetry indices	WHOLE GROUP (N= 46)	GROUP I with normal glucose values (N= 29)	GROUP II with hyperglycemia in the third trimester of pregnancy (N= 17)	p
Abdominal Circumference (mm)	330±31.50 Min: 248.2 Max: 389.3	328.81±35.17 Min: 248.2 Max: 362.9	336.03±27.06 Min: 315.5 Max: 389.3	0.05
Estimated fetal weight (g)	3224.64±544.96 Min: 2150 Max: 4300	3169.25±492.41 Min: 2150 Max: 3700	3275.77±604.83 Min: 2332 Max: 4300	0.2
Resistive index of umbilical artery	0.55±0.08 Min: 0.42 Max: 0.77	0.53±0.08 Min: 0.42 Max: 0.65	0.56±0.09 Min: 0.44 Max: 0.77	0.6
Resistive index of middle cerebral artery	0.73±0.06 Min: 0.56 Max: 0.86	0.73±0.04 Min: 0.67 Max: 0.8	0.72±0.08 Min: 0.56 Max: 0.86	0.7



**Figure 2.** The correlation between third trimester glycemia and abdominal circumference.

We detected a positive linear correlation between the third trimester blood glucose and the fetal abdominal circumference (AC) measured during the third semester ultrasound examination ( $r=0.32$ ,  $p<0.05$ ) as shown in [Figure 2](#).

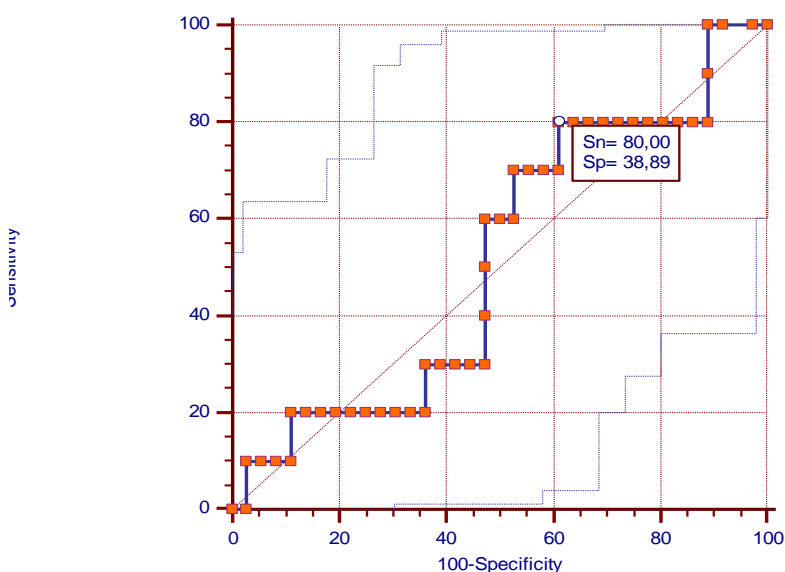
No significant correlations between third trimester glycemia value and ultrasound appreciated weight (on the basis of fetal biometry) and Doppler velocimetry indices determined by ultrasound examination before giving birth were found.

Analyzing the two groups we have found that the average weight of the newborns was

higher in the group with normal third trimester glycemia values ( $3593.10 \pm 483.97$ ), than in the group with third trimester hyperglycemia ( $3429.41 \pm 531.23$ ), but the difference was not statistically significant ([Table 4](#)).

**Table 4.** Fetal birth weight and birth type for the two study groups.

	WHOLE GROUP (N= 46)	GROUP I with normal glucose values (N= 29)	GROUP II with hyperglycemia in the third trimester of pregnancy (N= 17)	p
FETAL BIRTH WEIGHT (g)	3532.60±502.46 Min: 2500 Max: 4800	3593.10±483.97 Min: 2500 Max: 4400	3429.41±531.23 Min: 2800 Max: 4800	0.20
MACROSOMIA	10 (21.46%)	7 (24.13%)	3 (17.64%)	
BIRTH TYPE	Spontaneous 31 C section 15	Spontaneous 18 (62.07%) C section 11 (37.93%)	Spontaneous 13 (76.47%) C section 4 (23.53%)	



**Figure 3.** ROC curve for appreciating macrosomia risk using the third trimester glycemia value.

In order to assess the clinic utility of maternal BG from the third trimester of pregnancy in predicting macrosomia risk, we used the ROC curve method. Two ROC curves were drawn in order to obtain Sensitivity (Sn), Specificity (Sp) and the cut-off values of glucose in detecting macrosomia risk (newborns with a weight over 4000 g); utility performance as a diagnostic test was appreciated according to the

positive predictive value (PPV), negative predictive value (NPV) and the area under the ROC curve as shown in [Figure 3](#). Using the value of the third trimester glycemia for appreciating macrosomia risk, the area under the ROC curve was of 0.517 (IC 95%= 0,365-0.666)

Specificity, sensitivity and the cut-off values of glycemia determined in the third trimester of

pregnancy for detecting macrosomia risk, respectively the utility as a diagnostic test appreciated from the point of view of positive

predictive value, negative predictive value and of the area under ROC curve are given in [Table 5](#).

**Table 5.** Specificity, sensitivity and cut-off values for the ROC curves.

CUT- OFF VALUE	PPV (95% CI)	NPV (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
49.5 mg/dl	21.7 (10.9- 36.4)	-	100.00% (69.2- 100.00)	0.0% (0.0- 9.7)
85 mg/dl	22.7 (7.8- 45.4)	79.2 (57.8- 92.9)	50.00% (18.7- 81.3)	52.78% (35.5- 69.6)
92 mg/dl	18.8 (4.0- 45.6)	76.7 (57.7- 90.1)	30.00% (6.7- 65.2)	63.89% (46.2- 79.2)
100 mg/dl	18.2 (2.3- 51.8)	77.1 (59.9- 89.6)	20.00% (2.5- 55.6)	75.00% (57.8- 87.9)

The best rate between specificity and sensitivity is observed at the cut-off value of 85 mg/dl. For this value PPV is of 22.7 (IC 95%: 7.8- 45.4). For the cut-off value of 92 mg/dl specificity increases with the decrease of sensitivity. Both cut-off values have a low PPV and an increased NPV. For the superior limit of glycemic values considered normal outside pregnancy the sensitivity of detecting macrosomia is of 20.0%, and for the inferior limit, of 49.5 mg/dl sensitivity is of 100.0%. Also it is to be noted that for the superior limit considered normal outside pregnancy (100 mg%), PPV is of 18.2 (IC 95%: 2.3- 51.8).

### Discussions

Blood glucose values considered to be normal in an uncomplicated pregnancy have not been yet settled. Thus, the few studies which have analysed glycemia modification during pregnancy have demonstrated that glycemia value initially decreases comparatively to un-pregnant women glycemia, with a tendency to slowly increase from the first trimester towards due date. Thus, Paretti and collaborators [2] have observed that the level of 24 hours average glycemia rises from 71.9 mg/dl at 28 weeks of gestations up to 78.3 mg/dl at 38 weeks of gestation. The relevance of the increased values from the third trimester of pregnancy isn't known. However, in different European studies,

the identification of gluoregulatory disorders from the last trimester of pregnancy has reduced maternal, fetal and neonatal risks [3,4].

Because this study included pregnant women with fasting glucose value in the first trimester over 126 mg/dl received dietary recommendations to control their BG.

By determining the postnatal glycemia of mothers who have given birth to macrosomic foetuses, it was discovered that fetal weight correlated with hyperglycemia from the last trimester of pregnancy, undetected by the routine screening of gestational diabetes [5].

Obesity is frequently associated with hyperglycemia outside pregnancy [6-8]. In our study, mother's BMI when taken into evidence influenced fetal birth weight.

The main fetal consequence of gestational diabetes is represented by macrosomia. In many studies [9,10] gestational diabetes has significantly increased the percent of C-section deliveries while treatment of gestational diabetes seems to decrease the risk of fetal macrosomia, which is the main recommendation for C-sections [11].

The small number of cases in our study didn't allow us to observe the impact of gestational diabetes over birth complications. From this point of view, our study isn't in accordance with other studies done in other countries [12-14]. The result is not statistically significant because there can be no sufficient

statistical power due to the small number of cases included in the study and therefore we cannot draw a definitive conclusion.

Fetal macrosomia, which represents the main cause of maternal and fetal perinatal morbidity, didn't correlate directly with the values of maternal glycemia from the third trimester. The use of glycemia before birth represents a test with a low accuracy in appreciating macrosomia risk, no matter of the cut-off value used. Though the early

identification of gestational diabetes lowers the risk of fetal macrosomia, it doesn't decrease C-section rate [15,16].

## Conclusions

Last trimester glycemia value cannot represent a predictive factor for fetal macrosomia and perinatal complications. Still, more in depth studies over maternal glucose metabolism are required for a better evaluation of the fetal growth.

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