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CONTRIBUTION OF MATERNAL OBESITY AND WEIGHT GAIN IN PREGNANCY TO THE OCCURRENCE OF GESTATIONAL DIABETES

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Abstract: An increase in prevalence of gestational diabetes mellitus (GDM) was observed using new diagnostic criteria. We evaluated the prevalence of GDM in a population of pregnant women (109 women with gestational age of 24-28 weeks) and risk factors for GDM, such as maternal obesity and weight gain. The evaluation of each patient included an oral glucose tolerance test (OGTT) using the new diagnostic criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) for GDM, 2D ultrasounds and the registration of risk factors. The prevalence of GDM in the age group ≥30 years was 11.9%, which is comparable to the results of other studies. The relative risk (RR) for GDM was 1.738 (95% CI 0.630-4.795) in women over 30 years and 3.782 (95% CI 1.127-12.686) in women over 35. Weight gain in the group with GDM was significantly higher than in the group that included pregnant women without GDM ($p < 0.01$). Considering the high risk of GDM with excessive gestational weight gain, educational nutrition programs should be established for the fertile-age population, not only to prevent obesity but also to prevent excessive weight gain during pregnancy.

Key words: gestational diabetes; oral glucose tolerance test; weight gain; obesity; fetal ultrasound

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INTRODUCTION

Diabetes mellitus has become one of the main public health issues due to the association of chronic complications determining increased cardiovascular mortality and invalidity. The prevalence of type 2 diabetes is increasing and affects all age categories, including teenagers among whom a dramatic increase has been noticed during the last decade (Dabelea et al., 2014). Another category of people who can develop type 2 diabetes is pregnant women with gestational diabetes (Ben Haroush et al., 2004), who frequently present perinatal events (O'Sullivan et al., 2011). The main risk factors for the occurrence of GDM are: age (25 years); obesity; pre-diabetes prior to

pregnancy; 1st degree relatives with type 2 diabetes; GDM in a previous pregnancy; macrosomia; premature birth; race ("nonwhite"; Kim et al., 2007). The importance of correct diagnosis and classification of GDM has been outlined by the IADPSG, following the results of the study Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) (Metzger et al., 2008). The reported data regarding the prevalence of gestational diabetes is very different from one country to another (1-14%) but the regional data has maximum importance for establishing a long-term prevention strategy (Wendlandet et al., 2012; Metzger et al., 2008).

The aim of this study was to analyze the prevalence of GDM in a population of pregnant women, using new diagnostic criteria and an assessment of risk factors for GDM such as maternal obesity and excessive weight gain.

PATIENTS AND METHODS

The prevalence of GDM in a population of pregnant women over a 6-month period was investigated. Screening for the detection of diabetes in pregnancy was performed at the "Nicolae Malaxa" Clinical Hospital, and included all women with confirmed intrauterine pregnancy who came at the Obstetrics-Gynecology Department and who met all the inclusion criteria: pregnant women over 18 years old, gestational age between 24-28 weeks, women who signed the informed consent.

Those excluded were pregnant women with diabetes mellitus prior to pregnancy, pregnant women with comorbidities under treatment, and recent surgical interventions. Patients included in the study provided written informed consent regarding participation in the study. The study group comprised 109 pregnant women, aged between 18 and 40 and between 24 and 28 weeks of gestation. Clinical examination provided data on height (cm) and weight (kg). The body mass index (BMI – kg/m^2) prior to pregnancy and the current BMI were calculated to provide weight gain data.

All pregnant women underwent OGTT with 75 g of glucose using the new diagnostic criteria for GDM (Wendland EM et al., 2012). GDM was confirmed when at least one of the following criteria was fulfilled: fasting plasma glucose ≥92 mg/dl (5.1 mmol/l); 1 hour ≥180 mg/dl (10.0 mmol/l); 2 hours ≥153 mg/dl (8.5 mmol/l). Other laboratory parameters were also considered: glycated hemoglobin (HbA1c), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides and fasting insulin levels. 2D ultrasound examination for fetal biometry and the assessment of fetal annexes was performed between 24 and 28 weeks of pregnancy by a single examiner.

Maternal risk factors for GDM such as the personal GDM history, pre-diabetes, 1st degree relatives with diabetes and pathological antecedents related to previous pregnancies were also considered.

Statistical analysis

Values were expressed as averages ± SD for normally distributed data. Comparisons between the groups were made using ANOVA for quantitative variables and the $\chi 2$ test for categorical variables. For the statistical processing, we used SPSS software (version 18.2010). RR was obtained with the formula: Prevent when exposed/Prevent when non-exposed. We have applied direct logistic regression in order to determine the impact of some factors on the probability of the occurrence

of gestational diabetes. The model contained 6 independent variables: current BMI, initial BMI, grade of placental maturity, the thickness of placenta, HDL level and intrapartum fetal weight. The prediction model comprising these factors was statistically significant $\chi 2$ (7, N=109) =38, 23, $p < 0.001$, showing that the model distinguishes between patients with GDM and individuals not diagnosed GDM.

RESULTS

The average age of the pregnant women was 28.28±3.67 years and GDM was diagnosed mainly in the age group 35-39 years, the age of most of the cases being over 30. In the present study, RR for GDM in women over 30 was 1.738 (95% CI 0.630-4.795) and that of women over 35 was 3.782 (95% CI 1.127-12.686). The gestation age of the pregnant women under study ranged between 24 and 28 weeks, with an average of 25.93±1.11 weeks.

The global prevalence of GDM is 11.9% (95% CI 5.82%-7.98%) and, compared to the gestation age, the most numerous cases of GDM were revealed in the 28th week of gestation. The most significant increase of plasma glucose was observed at 1 h (166.77±10.24 versus 133.10±11.02) as compared to non-diabetic women ($p < 0.0001$).

The average level of HbA1c in patients with GDM was significantly higher than in individuals

Table 1. Characteristics of studied pregnant women stratified into diabetic patients (GDM+) and non-diabetic individuals (GDM-).

Characteristics of groups	GDM+ (n=13) mean ± SD	GDM – (n=96) mean ± SD	P
Age (years)	29.69 ± 4.83	28.08 ± 3.47	0.225
Pregnancy age (weeks)	26.31 ± 1.31	25.88 ± 1.07	0.242
Parity number	1.31 ± 0.48	1.38 ± 0.52	0.710
Weight gain (kg)	15.15 ± 9.32	7.78 ± 6.19	0.001
Initial BMI (kg/m^2)	21.85 ± 4.14	21.37 ± 3.14	0.978
Weight gain over allowed limits (%)	69.2%	29.2%	0.009
Fetal weight (g)	1006.62 ± 144.81	910.54 ± 119.09	0.015
Placenta (cm)	3.35 ± 0.82	2.73 ± 0.53	0.012
Fasting blood glucose (mg/dl)	93.62 ± 28.62	82.78 ± 8.74	0.277
Blood glucose after 1 h (mg/dl)	166.77 ± 10.24	133.10 ± 11.02	< 0.0001
Blood glucose after 2 h (mg/dl)	130.46± 47.34	109.95 ± 14.22	0.067
Insulin (μU/ml)	9.39 ± 6.91	10.47 ± 9.70	0.081
HbA1c (%)	6.81 ± 0.48	5.38 ± 0.31	0.000
Cholesterol (mg/dl)	225.77 ± 38.22	226.26 ± 49.96	0.677
Triglycerides (mg/dl)	186.54 ± 63.39	177.33 ± 60.50	0.687
HDL - C (mg/dl)	81.00 ± 9.70	68.23 ± 14.29	0.002
LDL - C (mg/dl)	161.38 ± 39.83	143.14 ± 27.75	0.061
HOMA-IR	2.24 ± 1.92	2.21 ± 2.01	0.275

Initial BMI (kg/mp) = pre-pregnancy body mass index; HbA1c(%) = glycated hemoglobin; HDL-C (mg/dl) = high density lipoprotein; LDL-C(mg/dl) = low density lipoprotein; HOMA-IR = homeostatic model assessment of insulin resistance.

not diagnosed GDM (p <0.0001); for total cholesterol, LDL, triglycerides, and homeostatic model assessment index of insulin resistance (HOMA-IR), no significant differences were found. Obesity was present in 3 of the 13 women with GDM and the average value of the BMI prior to pregnancy was not significantly different in the group of women with GDM as compared to that without GDM (p = 0.978). Weight gain in the group with GDM was significantly higher compared to the group of pregnant women without GDM (p=0.001). The optimum weight gain was established based on other studies and depended on the BMI prior pregnancy (IOM, 1992; Lederman, 1997). From the second trimester of pregnancy the recommended weight gain of is +500 g/week if BMI = 20 kg/m^2; +400 g/week if BMI = 20–25 kg/m^2; +300 g/week if BMI = 25kg/m^2. We considered abnormal any weight gain over these recommended limits.

In this study, we found a significant association between GDM and weight gain over the allowed limits, gestational diabetes being 5.46 times more frequent in patients with a weight gain over the allowed limits (p = 0.009). Fetal weight, monitored by intrapartum ultrasound assessment, in the group with GDM was significantly higher than in the group without diabetes (p = 0.015). Most of the women with GDM (n = 12 out of 13 with GDM) required only a diet change, and only one of them needed insulin therapy.

DISCUSSION

GDM prevalence is difficult to evaluate due to the different diagnostic criteria and population particularities. The use of new diagnostic criteria of GDM, which accepts the change of a unique value of plasma glucose during the OGTT, will determine an increase in GDM prevalence. The results obtained in our study highlighted a significant increase in plasma glucose more frequently at 1 h within OGTT as compared to non-diabetic women. This unique change of plasma glucose especially at 1 h has been reported in other studies (Metzger et al., 2008), and may explain the increase in GDM prevalence. The value of HbA1c has been found to be significantly higher in patients with GDM as compared to those without GDM but HbA1c cannot be used for screening, as it is not an accepted diagnostic criterion for GDM (ADA, 2014). The American Diabetes Association (ADA) recognizes and anticipates the significant increase of GDM incidence by using the new IADPSG diagnostic criteria. In the current study, GDM prevalence was 11.9% using the new diagnostic criteria as compared to the highest prevalence reported for Europe, probably due to a similar population structure. In Ireland the GDM prevalence using IADPSG criteria was 12.4% (O'Sullivan et al., 2012) and in France 12.1% (Schneider et al., 2010; Buckley et al., 2012). An increase in GDM prevalence in Europe of ~10% using the new diagnostic criteria as compared to 2-6% appreciated through classic criteria was reported. Numerous risk factors have been incriminated for the occurrence of GDM (Kim et al., 2007), but only maternal obesity and excess weight gain can be corrected. The estimate of the real prevalence of GDM and the identification of some susceptible to influence risk factors provide useful data for the establishment of prevention programs.

The main risk factors identified by us for GDM prevalence have been older age and increased weight gain in the mother. GDM prevalence significantly increased by age and the highest RR was in women over 35. Similar data have also been reported in other studies (Metzger BE et al., 2001; Xiong X et al., 2002).

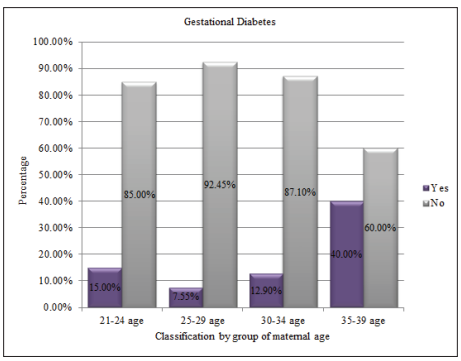

Fig. 1. Distribution of pregnant subjects by age (years).

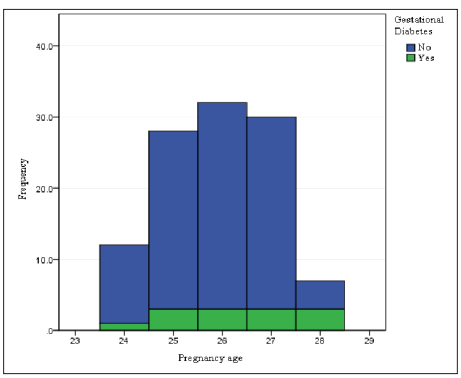

Fig. 2. Distribution of pregnant subjects by gestational age (weeks).

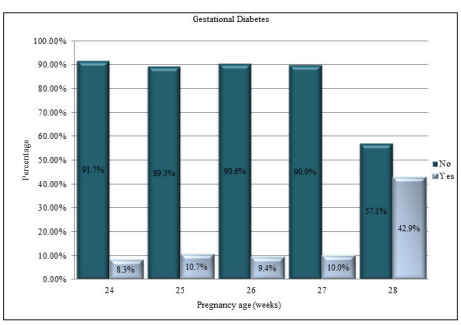

Fig. 3. Prevalence of GDM by gestational age (weeks).

Lao et al. (2001) reports that pregnant women aged between 35-40 have increased risk compared to younger women. Numerous studies have linked maternal obesity prior to pregnancy to GDM (Torloni et al., 2009; Seshiah et al., 2008). Jang et al. (1998) reported a statistically significant difference between the BMI prior to pregnancy in women with and without GDM. Although the average value of BMI prior to pregnancy in our study was not statistically significantly different in the groups of women with or without GDM, 23% of women with GDM were obese prior to pregnancy. This finding supports the link between maternal obesity and GDM. It is known that women with GDM have an excessive weight gain, probably because of a symbiosis with nutritional and gestational factors (Gibson et al., 2012; Radesky et al., 2008). Hedderson et al. (2010) even estimated a relation between the risk of occurrence of GDM and the weight gain rate. Compared with the lowest tertile of gestational weight gain rate (270 g/week), weight gains of 270-400 g/week and 400 g/week were associated with increased risk of GDM.

We found a significant association between the risk of occurrence of GDM and excessive weight gain in relation to prior BMI. The optimum weight gain has been established based on numerous studies (Abrams et al., 2000; Cedergren et al., 2006), it has been correlated to reduced incidence of perinatal outcomes and dependence on the BMI prior to pregnancy (IOM, 1992; Lederman et al., 1997). Excessive weight gain may be prevented by promoting life-style changes (diet recommendations, physical exercise), and the careful monitoring of pregnant woman (Tieu et al., 2008; Ferrara et al., 2011). Obesity during pregnancy and GDM are risk factors for giving birth to babies that are large for gestational age (LGA) (Ananth, 2002). Fetal weight, monitored intrapartum with 2D ultrasound, in our group of women with GDM, was significantly higher ($p = 0.015$) as compared to non-diabetic women, probably because of the exposure to hyperglycemia. An increase in thickness of the placenta was observed by ultrasound in our study, being directly proportional to the absence of maturity of chorionic villi by the increase in diameter of villous lumen (Gibson et al., 2012).

Increased fetal weight as well as thicker placenta are associated in our study to postprandial hyperglycemia, respectively to HbA1c, which was significantly increased in women with GDM, while for the level of serum lipids and HOMA index no statistically significant differences were noted. In other studies, the parity has been associated to the increased prevalence of GDM (Zargar et al., 2004).

This study updates the GDM prevalence data and supports the need to elaborate national screening strategies for this pathology, using the new diagnostic criteria. Considering the high risk of GDM associated to weight excess, nutritional education programs are required for the fertile-age population, not only to prevent obesity in general but, in particular, to prevent excessive weight gain during pregnancy.

Authors' contribution: CT conceived of the study, participated in design of the study, carried out all analyses and drafted the manuscript. CD participated in design of the study, selected the relevant data and reviewed the manuscript. FI participated in screening process and constructed the relevant datasets. ER participated in conception of the study and reviewed the manuscript. AE participated in screening process and reviewed the manuscript. GR participated in design of the study and reviewed the manuscript.

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