Full Length Research Paper

Gestational diabetes and perinatal outcomes: A case control study.

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The objective of this study was assessing the prevalence and the perinatal risk of Gestational Diabetes Mellitus (GDM). It's a case control methodology in which carriers of GDM were considered to be all pregnant women that during pre-natal care presented any degree of intolerance to glucose with beginning or diagnosis established for the first time during pregnancy. Maternal, obstetric and newborns variables were assessed. A significant statistical association was observed between the GDM group and the variables maternal age, body mass index, weight gain, parity, prenatal care, hypertensive syndrome, Apgar score at 1', birth weight, breech presentation, cesarean section, need for treatment in neonatal intensive care unit and fetal macrosomia. In conclusion, perinatal risk in GDM cases is associated with greater morbidity.

Keywords: Gestational diabetes mellitus, prevalence, perinatal outcome.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with beginning or diagnosis established for the first time during pregnancy (ADA, 2011; Metzger et al., 2010). The prevalence varies from 1% to 14%, depending on the population and the diagnostic methods performed (2004).

In GDM, as of the third trimester, the placenta is mature and secretes diabetogenic hormones which regress, in most cases, after delivery (Reichelt, 2002). Due to the fact of glucose passing freely through the placental barrier and insulin not presenting the same characteristic, mild hyperglycemias may cause congenital defects and early abortions since the fetal beta pancreatic cells do not produce insulin until the 12th week (Kelly et al., 2005). After this gestational period, the fetus appears to respond to hyperglycemia, producing elevated levels of insulin,

which, for their part, have properties of inducing growth and genetic defects (Kelly et al., 2005). Among the most commonly observed perinatal complications, the following stand out: neonatal hypoglycemia; macrosomia; congenital defects; mainly heart malformations; increase of cesarean section rates; shoulder dystocia and perinatal morbidity and mortality (2009).

The greater importance of studies about GDM is that with more information and knowledge is possible improve care provided to pregnant women with the disease, which contributes to better health care and consequently, better maternal and neonatal outcomes. Therefore, the objective of this study was to assess the prevalence of GDM and the perinatal risk induced by this metabolic illness.

MATERIALS AND METHODS

This is a case control study with pregnant women admitted at the Obstetrics and Gynecology Department of

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the General Hospital of Caxias do Sul (GHCS), from March/1998 to December/2008. Data was obtained from structured and specific medical records which are part of the routine services to pregnant women and newborns, both in the Obstetric Unit and in the Neonatal Intensive Care Unit (NICU).

Study population

The population assessed was divided into two groups: (1) cases – pregnant women with a clinical diagnostic and laboratory proven GDM; (2) controls – pregnant women whose gestational evolution has not presented any clinical or laboratory alteration compatible with GDM. For each case selected, two controls were included, corresponding to the two subsequent births. The research project was approved by the Ethics in Research Committee of the Caxias do Sul University on the protocol number 339/2010.

Variables analyzed

1- Maternal and obstetric: age (years); schooling (years of study); previous stillbirth; body mass index (BMI), calculated as of the weight of the pregnant woman at the beginning of pregnancy according to World Health Organization (WHO) and the Quetelet index (weight [kg] divided by height [m] squared): underweight (BMI<18.5 kg/m^2), norm weight (18.5 kg/m^2 to <25 kg/m^2), pre-obesity (25 kg/m^2 to <30 kg/m^2), and obesity (>30 kg/m^2); classification of pregnant women according to Nucci et al. (2001); weight gain calculated according to the Cedergren criteria (2006); parity; number of prenatal care visits; hypertensive syndrome (composite of chronic hypertension, mild and severe preeclampsia, chronic hypertension plus severe superimposed preeclampsia, gestational hypertension).

2- Newborns: 1 and 5-min Apgar score (identified by staff neonatologist); umbilical artery pH; birth weight (g); gestational age (wks), based on the first day of the last menstrual period and early ultrasound; breech presentation at birth; cesarean section rate; fetal mortality rate; neonatal intensive care admissions; early neonatal mortality rate (less seven days); macrosomia (fetal weight ≥4,000g or above the 90th percentile for gestational age) (Battaglia and Lubchenco, 1967); congenital defects.

Blood samples through checking of the arterial pH were obtained in the umbilical artery and were collected immediately after birth (Madi, 2003).

Inclusion and exclusion criteria

Gestational age of ≥20 weeks were included in the study, with GDM diagnosis established by 75g oral glucose tolerance test (OGTT 75g) according to Brazilian Diabetes Society and approved by the World Health Organization (Miranda, 2006). Patients with Type 1 or 2 Diabetes Mellitus prior to pregnancy, gestational age ≤20 weeks and pregnant women who gave birth at home or in another institution were excluded from the study.

Statistical analysis

Statistical analysis was undertaken with SPSS program (Statistical Package for the Social Sciences) version 17.0. The two groups were compared in accordance to the variables studied. For statistical analysis, the means, standards deviations and Student T test and Mann-Whitney test were used for numerical variables, chi-squared tests for categorical values and risk estimate by the Odds Ratio (OR) with IC 95%. The (alpha) significance level adopted was 5%.

RESULTS

The GHCS is reference hospital for high risk pregnancy in Unique System of Health of Caxias do Sul city and of the 50 cities of the 5th Health Coordination Office of RS state.

In the period of study, 15,153 births were identified. Among them, 197 (1.3%) were related to the clinical and laboratory diagnosis of GDM. The control group was composed of 392 (2.6%) births occurred after GDM group, but without the characteristics of the metabolic disease.

The maternal characteristics of the sample analyzed are presented in Table 1. The patients included in the GDM group were characterized by presenting a greater average of age, pre-gestational weight, parity and number of pre-natal visits than the control group. In addition, they developed hypertensive disorders with a greater frequency.

Table 2 shows the perinatal characteristics. It may be observed that there was no significant statistical difference between the groups in regard to gestational age at the time of birth. The newborns included in GDM group were characterized by presenting a lower 1-min Apgar score, even when recovery of the vitality may be verified at the time of analysis of 5-min Apgar score. The

Table 1: Distribution of maternal and obstetric characteristics (n=589) of the General Hospital of Caxias do Sul, RS, 1998-2008.

Maternal and obstetric variables	GDM n=197	Control n=392	p	OR (IC95%)
Age (years) [¶]	31.6±6.9	25.1±6.5	<0.0001	
>35	100 (50.7%)	44 (11.1%)	<0.0001	8.2 (5.3-12.7)
Schooling [§]			NS	
≤8 years	131 (72.8%)	268 (68.3%)		
>8 years	49 (27.2%)	125 (31.7%)		
Previous stillbirth [§]	11 (5.6%)	10 (2.5%)	NS	
BMI [¶]	22.9±5.2	19.4±4.1	<0.001	
Underweight [§]	30 (21%)	199 (51.4%)		
Normal [§]	71 (49.7%)	151 (39%)	NS	
Overweight [§]	28 (19.9%)	28 (7.2%)	<0.005	2.2 (1.2-3.9)
Morbid obesity [§]	14 (9.8%)	9 (2.4%)	<0.004	3.3 (1.3-8.3)
Weight gain [¶]	8.9±6.1	12.2±5.6	<0.001	
Parity (µ)	1.9	1.1	<0.001	
Pre-natal care (# visits)[¶]	10.1±4.9	7.5±3.1	<0.001	
Hypertensive syndrome [§]	45 (22.8%)	44 (11.2%)	<0.0001	2.3 (1.5-3.8)

NS: not significant; µ: means; BMI: Body Mass Index [20]; [¶]: means±standard deviation; [§]: results expressed in absolute number and percentage; Hypertensive syndrome: composite of chronic hypertension, mild and severe preeclampsia, chronic hypertension plus severe superimposed preeclampsia, gestational hypertension.

Table 2: Distribution of the neonatal characteristics (n=589) of the General Hospital of Caxias do Sul, RS, 1998-2008.

Neonatal variables	GDM n=197	Control n=392	P	OR (IC95%)
Apgar score [¶]				
1'	7.11±2.2	7.66±1.9	<0.002	
5'	8.62±1.4	8.87±1.5	NS	
pH umbilical artery [¶]	7.21±0.1	7.22±0.4	NS	
Birth weight (g) [¶]	3,265,9±714,9	3,074.3±644,3	<0.001	
GA (weeks) [¶]	38.4±1.8 (31-41.6)	38.6±2.3 (25-42)	NS	
Breech presentation [§]	13 (6.7%)	11 (2.8%)	<0.03	2.4(1.0-5.9)
Cesarean section [§]	89 (45.9%)	133 (34.1%)	<0.008	1.6(1.1-2.3)
Stillborn [§]	5 (2.5%)	5 (1.3%)	NS	
NICU [§]	49 (24.9%)	45 (11.5%)	<0.001	2.5(1.6-4.1)
Neonatal mortality [§]	0	1(0,3%)		
Fetal macrosomia [&]	64 (35,8%)	56 (15%)	<0,0001	2,9(1,9-4,4)
Congenital malformations [§]	8 (4,1%)	0		

NS: not significant; [¶]: results expressed in means±standard deviation; [§]: results expressed in absolute numbers and percentages; GA: gestational age with upper and lower limits; NICU: need for treatment in neonatal intensive care unit; [&] fetal macrosomia: birth weight ≥4,000g.

acidosis related to the low score of 1-min Apgar score was not confirmed by the umbilical artery pH analysis. In the GDM group, a greater percentage of fetuses with greater birth weight, breech presentation, cesarean section rate, neonatal intensive care admissions, fetal macrosomia and congenital malformations was observed.

Table 3 shows the causes of newborn hospitalization in neonatal intensive care unit. A greater prevalence of

Table 3: Cause of hospitalization of the newborn in NICU (n=49) of the General Hospital of Caxias do Sul, RS, 1998-2008.

Causes of hospitalization	GDM (n=49)	Control (n=45)	p	OR IC95%
Prematurity [§]	15 (30.6%)	20 (44.4%)	NS	0.6 (0.2-1.4)
General symptoms				
Respiratory dysfunction[§]	8 (16.3%)	5 (11.1%)	NS	1.6 (0.4-6.1)
Transitory tachypnea [§]	3 (6.1%)	2 (4.4%)	NS	1.4 (0.2-12.7)
Hypoglycemia [§]	8 (16.3%)	6 (13.3%)	NS	1.3 (0.4-4.6)
Anoxia [§]	6 (12.2%)	5 (11.2%)	NS	1.1 (0.3-4.7)
MAS [§]	5 (10.3%)	4 (8.9%)	NS	1.2 (0.3-5.6)
Hyaline membrane [§]	1 (2.1%)	1 (2.2%)	NS	
Jaundice [§]	3 (6.1%)	2 (4.5%)	NS	1.4 (0.2-12.7)

NS: not significant; §: results expressed in absolute numbers and percentages; NICU: need for treatment in a neonatal intensive care unit; MAS: Meconium Aspiration Syndrome.

respiratory dysfunctions, transitory tachypneia and hypoglycemia in newborn of diabetic mothers may be observed.

DISCUSSION

In the study, the prevalence of GDM was 1.3% (n=197). Upon comparing those data with those in the literature, it was observed that the prevalence of the disease may vary from 1.2% to 14.3% (2001), depending on the test undertaken form diagnosis and the characteristics of the population assessed. However, the information related to this question is controversial. Lawrence et al. (2008) cited that the prevalence of the GDM is found to be stable, but, in contrast, an increase in the rates of pre-existing DM1 and DM2 has been verified, variables that seem not to depend on ethnicity.

It was seen that the pregnant women carriers of GDM were characterized as presenting a greater prevalence of some of the risk factor known for the pathology: age, weight and parity, macrosomia and a previous stillbirth (Reichelt, 2002). These conditions corroborate that described in the Project Directives of the Brazilian Medical Association and of the Federal Medical Council (Miranda, 2006), even though the parity observed in the study (1.9 *vs.*1.1; in the GDM and control group respectively; p<0.001) is not a commonly described characteristic in the studies related to the disease (Kieffer et al., 2006). This association may be explained by the greater average age among the pregnant women who are carriers of the metabolic disturbance (Kieffer et al., 2006).

Kieffer et al. (2006) suggested that there is no association between the degree of schooling and the levels of maternal glycemia. In the GHCS study, the schooling variable appeared in a similar way in both groups assessed. The same author report an average maternal age of 28.6 years, while in the study, the average age was seen to be 31.6 years *vs.* 25.1 years in the control population. It was also observed that the pregnant women with an age ≥35 years were 4.5 fourfold present in the GDM group than in the control group.

Macrosomia can occur in up to 50% of the pregnant women with GDM (Montenegro, 2001). This fact seems to be related to the increased levels of maternal glycemia, to the elevated BMI prior to pregnancy and to maternal age greater than 40 years old (Kelly et al., 2005). In the study, the prevalence of fetal macrosomia was 35.8% vs. 15% in the control group. Excessive fetal growth is the most common adverse effect cited in patients with GDM. It is related to the rate of fetal hyperinsulinemia induced by maternal hyperglycemia and nutrients that cross the placental barrier. The macrosomia is correlated to important repercussions, namely: increase in the risk of fetal death, fetal birth injury, dystocia, neonatal hypoglycemia, congenital malformations and increased cesarean section rates, cesarean section and forceps delivery (Montenegro, 2001). In the study, the birth weight in GDM and control groups were 3,265.9±714.9 grams and 3,074.3±644.3 grams, respectively.

Pregnant women with GDM present increased rates of cesarean section. Most studies report an average incidence of 30%. It is reported that what influences these rates is the judgment and expectations of the physician. Thus, Mires et al. (1999) reported that obstetric staff that was aware of the pregnant woman's disease indicated 50% more cesarean sections than obstetrician who were not aware of the diagnosis,

regardless of birth weight. In the study, the cesarean section rate was 45.9% vs. 34.1% in the control group. The most prevalent indications were previous cesarean section, hypertensive syndrome, intrapartum fetal distress, breech presentation and macrosomia.

In the study, the congenital malformation rates do not differ from those observed in the general population (3%) (Kelly et al., 2005). It was observed eight cases (4.1%), with three cases being observed in the genitourinary tract and three in the central nervous system. The gastrointestinal tract and muscular skeletal system contributed with one case each. In the control group, no type of malformation was observed. No cases of malformation of the cardiovascular apparatus were identified in the GDM group.

According to literature, it is estimated that the risk of developing GDM is approximately 2, 4 and 8 times greater in pregnant women who are overweight, obese and morbidly obese respectively, when compared to the population of appropriate weight (Chu et al., 2007). It is reported that in United States, 30.5% of patients begin pre-natal care with degree 2 and 3 obesity (Chu et al., 2007). In South Africa, this rate is 44%. It is reported that 42% of the pregnant women carriers of GDM began pregnancy overweight or obese (Basu et al., 2010). In the study, considering the same group of pregnant women, 29.7% began pre-natal care with BMI≥25. At the same time, it was seen that these same patients presented less weight gain than the control group at the end of the pregnancy (8.9±6.1 vs. 12.2±5.6). It is believed that these results may be related to the greater number of pre-natal visits (10.1±4.9 vs. 7.5±3.1) performed in a specific outpatient area of the GHCS, and the better orientation undertaken by a multidisciplinary team. Late beginning of pre-natal visits seems to be related to worse maternal and perinatal outcome (Kieffer et al., 2006). Reichelt et al. (2002) suggested that obesity and excessive weight gain in pregnancy are risk factors for GDM.

The preeclampsia rates seem to be associated with those of GDM, increasing with the increased levels of glycemia. HAPO study (Yogev et al., 2010) showed a linear relationship between elevated BMI and preeclampsia. In the study, 22.8% (n=45) of the patients who were carriers of GDM presented some type of hypertensive disease. Stone et al. (1994) showed a 3.5 times greater risk of hypertensive disease among pregnant women with BMI≥32.3kg/m^2 when compared to pregnant women with a lower BMI. It is fitting to emphasize that the increase in the prevalence of hypertensive syndrome in patients with GDM is associated with a higher maternal age range.

The reduction of perinatal mortality seems to arise from the good quality of assistance in this period (Kelly et al.,

2005) and effective therapeutic intervention (2002). In accordance with Table 2, the study presents a similar perinatal mortality rate between the two groups studied. It is necessary that the pre-natal care be more carefully applied so as to minimize maternal death at childbirth and fetal and neonatal morbidity (Kautzky-Willer et al., 2004). The current rates of perinatal mortality observed suggest that a minimum mortality rate may be reached; however, great difficulties in access to care and treatments may result in increased rates of perinatal mortality, a fact that appears to interfere in pregnancies complicated by diabetes.

Yang X et al. (2002), showed an increased chance of breech presentation [OR 3.47; IC95% (1.1–10.8); 8.8% vs. 3.6%; p<0.03]. Data is similar to that identified in the study under discussion, since the prevalence of breech presentation in the GDM group was 6.7% vs. 2.8% in the control group (p<0.03).

Weiner (1988), observed a greater number of newborns with Apgar score <7 in the 1st minute of life in the GDM group than in the control group. Jensen et al. (2000), upon analyzing the Apgar score <7 in the 5th minute, did not identify a difference between the two groups. The results observed in the study are similar to the two studies cited previously, even though in the GDM group a lower score in the 1st minute than in the 5th minute is identified in the GDM group (7.11±2.2 vs. 7.66±1.9; p<0.002, respectively). In the sequence, in the 5th minute, a rapid recovery of the newborn of both groups was observed, not verifying a statistically significant difference between them. Jensen et al. (2000) showed that children of patients with GDM had greater need of neonatal intensive care admission than the control group (46.2% vs. 11.9%; p<0.001), with these results being similar to those of the study under discussion (24.4% vs. 11.5%; p<0.001). In the study, the analysis of the means of the pH in the blood of the umbilical artery in the two study groups was not associated with fetal acidosis (pH<7.1).

CONCLUSION

In conclusion, the prevalence of the GDM in current study was 1.3%. The GDM was associated with lower 1-min Apgar score, as well as higher rates of macrosomia, breech delivery, cesarean section rates and neonatal intensive care admissions. On the other hand, an association between the disease and the level of schooling, previous stillbirth, low Apgar indexes at the 5th minute, pH in the blood of the umbilical artery less than 7.1, and fetal mortality in the current pregnancy were not observed.

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