Pregnancy outcomes and medical costs according to gestational diabetes mellitus diagnostic criteria: randomized prospective study. POMEC study.

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Due to Hyperglycemia and Adverse Pregnancy Outcomes study results, a new gestational diabetes mellitus (GDM) diagnostic criteria was defined using a one-step approach (75-g oral glucose tolerance test -OGTT-) [1]

However, not all scientific societies have accepted and have implanted this new diagnostic criteria. The lowest glycemia cut-off of this criteria regarding the two-step approach entails an increase in GDM incidence with discordant studies about its cost-effectivity [2–4].

It will be assessed if pregnancy outcomes and medical costs are different depending on diagnostic criteria used.

RESEARCH DESIGN AND METHODS

The POMEC study is a randomized, parallel group trial, conducted in Spain. The Ethics Committee at Hospital Universitari Mútua Terrassa (Spain) approved the study.

Participants:
All pregnant women with follow-up of their gestation at Hospital Universitari Mútua Terrassa (Spain), at first antenatal visit, will be proposed to participate in the study.

Inclusion Criteria:
- Age 18-50 years
- No expectation that the participant will be moving out of the area of the clinical centre during the next year
- Informed Consent Form signed by the subject

Exclusion Criteria:
- Pre-existing type 1 or 2 diabetes
- Advanced human immunodeficiency virus infection (on medications that cause hyperglycemia), severe liver disease, gastric bypass surgery or other illnesses/surgeries that preclude them from drinking the glucose solution.

Randomization:

All pregnant women without a former diagnosis of diabetes mellitus will be considered for gestational diabetes mellitus (GDM) screening at 24–28 weeks of gestation.

Women with risk factors for diabetes at their initial prenatal visit will be screening at 9-12 weeks of gestation. Risk factors are: Age >35years, obesity (body mass index ≥30kg/m^2 or >27.5kg/m^2 in Asian Americans), first-degree relative with diabetes and high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander).

At the time of GDM screening, patients will be assigned a number by a random number generation program (ratio 1: 1) that will classify them to one of the following two groups:
- Experimental Group (One-step): International Association of Diabetes and Pregnancy Study Groups (IADPSG) Criteria.
Perfoming a fasting 2 hour 75g OGTT. The diagnosis of GDM is made if at least one or more values are ≥: Fasting 92, 1-hour 180, or 2-hour 153 mg/dL.

- Active Comparator (Two-step): National Diabetes Data Group (NDDG) Criteria
Step 1: Performing a 1h 50-g glucose load test (nonfasting). If the plasma glucose level measured 1 h after the load is ≥140 mg/dL, proceed to a 100-g OGTT.
Step 2: 100-g OGTT. The diagnosis of GDM is made if at least two of the following four plasma glucose levels measured (fasting, 1 h, 2 h, 3 h after the OGTT) are ≥: 105mg/dl, 190mg/dl, 165mg/dl and 145mg/dl respectively.
If only one value is exceed, 100g OGTT will be repeated 2-3weeks after.

Pregnant women without GDM diagnosis at third trimester of pregnancy will repeat GDM screening (according previous randomization) if it appears macrosomia or/and polyhydramnios in the follow-up.

GDM diagnosed women will be managed with diet and self-monitoring of blood glucose. Insulin will be added according to the local protocol[5]. All women will receive routine prenatal care (without differences between randomized groups).

Outcomes
Primary outcome Measures:

Large for gestational age (LGA): Infant birthweight >90th centile using customized growth curves. Time Frame: At birth of infant.

Secondary Outcome Measures:

1. Infant outcomes

- Small for gestational age (infant birthweight <10th centile using customized growth curves); macrosomia (infant birthweight >=4kg), Neonatal obstetric trauma (shoulder dystocia, clavicle fracture, brachial plexus injury, intrapartum asphyxia), Congenital anomalies (Coding of EUROCAT), Pregnancy loss (Miscarriage, stillbirth, neonatal death)

Time Frame: At birth of infant

- Neonatal hypoglycaemia (neonatal plasma glucose levels <2.5 mmol/L in the first 24 hours of life and <2.8 mmol/L thereafter), Neonatal hypocalcemia (neonatal calcium levels <7mg/dl), Neonatal hyperbilirubinemia (hyperbilirubinemia treated with phototherapy), Neonatal polycythemia (hematocrit from a peripheral venous sample >65 percent), Respiratory Distress Syndrome (onset of progressive respiratory failure shortly after birth, in conjunction with a characteristic chest radiograph -after ruling out other causes-), Hypertrophic cardiomyopathy (increased left ventricular –LV- wall

thickness ≥15 mm imaged anywhere in the LV wall -by transthoracic echocardiography-), NICU admission (NICU admission for treatment or surveillance), neonatal hospital stay (Length of hospital stay –days-).

Time Frame: at infant hospital discharge.

- Perinatal mortality (infant deaths that happen at less than 7 days of age and fetal deaths with a gestational age of 28 weeks or more). Time Frame: First 7 days postpartum.

2. Maternal outcomes

-Hypertension in pregnant: worsening of chronic hypertension, gestational hypertension and preeclampsia. Time Frame: First 3 months postpartum

- Polyhydramnios (Amniotic fluid index ≥25 cm). Time Frame: At birth of infant.

- Cesarean section delivery of a baby through a surgical incision in the mother's abdomen and uterus. Time Frame: At birth of infant.

- Maternal hospital stay: Length of hospital stay (days). Time Frame: at maternal hospital discharge.

- Questionnaires: Evaluation of Mediterranean diet adherence using Mediterranean Diet Adherence Screener (MEDAS) questionnaire. Evaluation of health-related physical activity using IPAQ questionnaire. Time Frame: up to 12-14weeks from last menstrual period.

3. Gestational age at delivery: Gestational age was defined as completed weeks based on last menstrual period or the earliest ultrasound assessment if discordant. Time Frame: At birth of infant.

4. Medical cost: economic cost include laboratory costs; glucose bottles (50 g, 100 g and 75 g); pharmaceutical expenditure (exact insulin doses consumed, total pens, needles, strips); medical visits during pregnancy and postpartum (endocrinologist, educational nurses, obstetrician and midwifes); total number of tests (ultrasounds, cardiotocography records); cost of intensive care unit admissions (Length of stay and complexity) and total hospital admission costs. Time Frame: First 3 months postpartum

Statistical analysis

Sample size (n=3,644) was calculated to detect a 20% decrease rate of LGA (primary outcome), assuming baseline rate of 16.5% (α=0.05 and β=0.80). This decrease rate was obtained from *St Carlos Gestational Diabetes Study*, carried out in Spanish population which compared Carpeten-Coustan criteria vs IADPSG criteria[3]. Since we will use NDDG criteria (vs. IADPSG), baseline LGA incidence was obtained from Spanish Multicentre Study[6].

Results will be presented as means ± standard deviation in normal distribution, median

[interquartile interval (IQI)] in non-normal distribution or percentages. Normal

distribution will be tested for each variable using the Kolmogorov test.

Student t test will be used for normally distributed variables and the Mann-Whitney U

test for non-normally distributed variables between two independent groups.

Proportions will be compared using a Pearson's chi-square or Fisher exact test as

appropriate.

We will use logistic regression analyses or multivariate linear regression (as appropriate) to estimate the ratio of the probability [I-TDS(1]of occurrence of an adverse event (primary and secondary outcomes) with 95% CIs by experimental group versus control group adjusting for cofounding factors (age, smoke habit, weight, multiparity)
P values <0.05 were considered statistically significant. All statistical calculations will be performed with the STATA 14.0 statistical package.

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