Gestational diabetes mellitus and risk of autism spectrum disorders in offspring: the prospective follow-up study

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BACKGROUND

The occurrence of gestational diabetes mellitus (GDM) is compatible with the prevalence of obesity, and these conditions have risen globally during recent years. Currently, among women of reproductive age, more than a third are obese, and an additional GDM up to 15% will develop during pregnancy.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by severe deficits in socialization, communication, and repetitive or unusual behaviors, affecting 1 in 68 children.

GDM has been associated with increased risk of ASD in children while the association between maternal pre-pregnancy obesity and ASD has been inconsistent. Although morbid obesity and GDM are highly comorbid, rarely have studies attempted to analyze their independent and combined effects on ASD. The combination of maternal obesity and GDM is associated with greater risk of ASD than either obesity or GDM alone, particularly when ASD co-occurred with intellectual disability (ID).

AIM

The aim of the study was to use birth cohort to

- (1) examine the independent and combined associations of maternal obesity and GDM with ASD in children,
- (2) analyze the effects of ID and attention-deficit/hyperactivity disorder (ADHD) in children with ASD.

METHOD

The cohort from the small community (n=17,000 inhabitants) was included in the prospective follow-up study. Twenty-six mother-child pairs where the pregnant women had had GDM (group 1) and received antenatal care at one of the Gynecology Clinic in Latvia from January 2014 through June 2016 were included in the study. They will be prospectively followed-up and compared with 26 mother-child pairs where the pregnant women had had morbid obesity (group 2).

According to the WHO, the diagnosis of GDM was made using a single-step 75 g oral glucose tolerance test (OGTT) when one or more of the following criteria were met during routine testing between weeks 24–28 of pregnancy: fasting plasma glucose 5.1–6.9 mmol/L; 1-hour post 75 g oral glucose load ≥ 10.0 mmol/L; 2-hour post 75 g oral glucose load 8.5–11.0 mmol/L.

Morbid obesity was diagnosed by determining BMI of 30 kg/m² or more. Data about child's medical condition were obtained via the retrospective review of medical records.

Standardized instruments including a parent interview (Autism Diagnostic Interview-Revised [ADI-R]), an observational scale (Pre-Linguistic Autism Diagnostic Observation Schedule/Autism Diagnostic Observation Schedule [ADOS]) will be used for follow-up study for ASD, and independent clinical diagnoses will be made at ages 2 and 9 years compared with a clinical research team's criterion standard diagnoses.

RESULTS

Mothers' average age in group 1 at the beginning of pregnancy was 30.8 $\pm$ 3.9 years and 29.2 $\pm$ 2.4 years in group 2. 39.1% (n=9) of women with GDM had had GDM in a previous pregnancy.

At the first antenatal visit, the mean maternal BMI ranged from 16.3 to 41.9 kg/m² and the diagnosis of morbid obesity was made in 26.9% (n=7) of women in group 1. BMI in group 2 showed values from 30.2 to 39.5 kg/m².

38.5% (n=10) of expectant women with GDM were consulted by endocrinologists during pregnancy. In group 1 nutrition counseling and physical activity as primary tools in the management of the disease was used in 69.2% (n=18) and 80.8% (n=21) of cases, respectively; in group 2–42.3 % (n=11) and 61.5% (n=16), respectively.

Post-partum endocrinology consultation and maternal glycemic status re-evaluation with a 75 g OGTT at 6–12 weeks after delivery received 19.2% (n=5) of GDM patients. The mean newborn birth weight was 3728.3 $\pm$ 928 g in GDM mothers and 3886 $\pm$ 754 g in mothers with morbid obesity. 11.5% (n=3) of women included in group 1 was primiparous, and 19.2% (n=5) of women included in group 2.

DISCUSSION

The findings suggest that children whose mothers had a combination of morbid obesity and GDM during pregnancy may have an elevated risk of developing ASD and ID.

Given the interaction the role of in utero imprinting in increasing the risk of neurodevelopmental disorder in the offspring of mother with pre-pregnancy morbid obesity or GDM, as well as increasing maternal and fetal vulnerability to other noncommunicable diseases, there is needs to be a greater focus on preventing, screening, diagnosing, and managing morbid obesity in pre-pregnancy as well, GDM and implementing programmes for neurodevelopmental disorder follow-up.

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