Growing evidence that maternal gestational diabetes increases risk of autism in offspring

Andrea L Roberts, Vy T Nguyen

Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA
Correspondence to Dr Andrea L Roberts, aroberts@hsph.harvard.edu

ABSTRACT FROM: Xiang AH, Wang X, Martinez MP, *et al*. Association of maternal diabetes with autism in offspring. *JAMA* 2015;313:1425–34.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Maternal gestational diabetes has been identified in several prior studies as being associated with elevated risk for autism spectrum disorder in offspring.[1–4] Maternal gestational diabetes has also been previously associated with impaired language development in offspring.[5] Maternal obesity, another indicator of the metabolic syndrome, has been associated with offspring autism in a prior study.[3] No studies have examined the timing of the onset of maternal gestational diabetes with respect to autism risk in offspring.

METHODS OF THE STUDY

This retrospective cohort study used medical record and birth certificate data from a racially and ethnically diverse health maintenance organisation to examine the association of pre-existing maternal type 2 diabetes and maternal gestational diabetes with offspring autism spectrum disorder. The study sample, comprised of more than 322 000 singleton children born in Kaiser Permanente Southern California (KPSC) hospitals between 1995 and 2009, is largely representative of the population of southern California in terms of race/ethnicity and socioeconomic position. Exclusion criteria included non-enrolment in the KPSC plan by age 1 year, congenital abnormalities, maternal type 1 diabetes and missing maternal and child data. The children were followed up for a median of 5.5 years after birth for clinical diagnosis of autism spectrum disorder that includes autistic disorders, Asperger syndrome, or pervasive developmental disorder not otherwise specified, ascertained through paediatric developmental specialist evaluations. In addition to exposure to pre-existing maternal diabetes, the time of onset of maternal gestational diabetes was assessed as a continuous variable and a categorical variable (26 weeks or earlier vs after 26 weeks). The relative risks of offspring autism spectrum disorder were estimated from Cox regression models adjusted for birth year and maternal and child characteristics as potential confounders.

WHAT DOES THIS PAPER ADD?

- This study elucidates the timing of onset of maternal gestational diabetes with respect to offspring autism risk. Owing to the detailed medical records used in the study, the researchers were able to identify an association of maternal gestational diabetes with offspring autism for gestational diabetes diagnosed by 26 weeks' gestation, but not after 26 weeks or in pre-existing maternal diabetes.
- Results are in keeping with neuropathology studies of brains of individuals with autism that suggest dysregulation of processes occur primarily in the first half of pregnancy, including neurogenesis, neuronal migration and neuronal maturation.[6]
- In a subset of the sample, a positive association of maternal pre-pregnancy body mass index and maternal gestational weight gain with offspring autism was also identified.

LIMITATIONS

- The association of maternal gestational diabetes with autism in offspring was substantially attenuated after adjustment for maternal age and other demographic factors, suggesting that there may be additional unmeasured confounding.
- It is possible that surveillance of offspring for autism differed among women with and without diabetes diagnosis, resulting in ascertainment bias, particularly since follow-up depended on continuous KPSC plan membership.

WHAT'S NEXT IN RESEARCH

Studies must now be conducted to assess whether interventions to reduce maternal gestational diabetes also lower risk of autism in offspring. Additionally, research must determine whether other indicators of maternal metabolic dysregulation, such as central adiposity, elevated triglycerides and elevated cholesterol, are associated with offspring autism. Further research is needed also to address paternal factors jointly with maternal factors. As mothers are often administratively simpler to follow than fathers, most studies of parental exposures in association with offspring health focus on maternal exposures and lack data on paternal exposures, resulting in possible bias.

DO THESE RESULTS CHANGE YOUR PRACTICES AND WHY?

Evidence that gestational diabetes may be a causal risk factor of autism spectrum disorder is sufficient that greater efforts must be made to reduce risk factors for gestational diabetes among women of childbearing age and prevent development of gestational diabetes in pregnant women. Women should be screened for gestational diabetes earlier in the pregnancy. Additional support should be provided to women of childbearing years to maintain a healthy weight, and women should be informed that their weight and weight-related health conditions may affect not only their health, but also the health of their children.

Competing interests None declared.

doi:10.1136/eb-2015-102142

Received 13 July 2015; Revised 16 September 2015; Accepted 17 September 2015

REFERENCES

1. **Burstyn I**, Sithole F, Zwaigenbaum L. Autism spectrum disorders, maternal characteristics and obstetric complications among singletons born in Alberta, Canada. *Chronic Dis Can* 2010;**30**:125–34.
2. **Lyall K**, Pauls DL, Spiegelman D, *et al*. Pregnancy complications and obstetric suboptimality as risk factors for autism spectrum disorders in children of the Nurses' Health Study II. *Autism Res* 2012;**5**:21–30.
3. **Krakowiak P**, Walker CK, Bremer AA, *et al*. Maternal metabolic conditions and risk for autism and other neurodevelopmental disorders. *Pediatrics* 2012;**129**:e1121–8.
4. **Xu G**, Jing J, Bowers K, *et al*. Maternal diabetes and the risk of autism spectrum disorders in the offspring: a systematic review and meta-analysis. *J Autism Dev Disord* 2014;**44**:766–75.
5. **Dionne G**, Boivin M, Séguin JR, *et al*. Gestational diabetes hinders language development in offspring. *Pediatrics* 2008;**122**:e1073–9.
6. **Lyall K**, Schmidt RJ, Hertz-Picciotto I. Maternal lifestyle and environmental risk factors for autism spectrum disorders. *Int J Epidemiol* 2014;**43**:443–64.