



46th Annual Scientific Meeting of the Nutrition Society of Australia, 29 November – 2 December 2022, Sustainable nutrition for a healthy life

Maternal diabetes in pregnancy and developmental programming of neurodevelopment disorders: An inflammatory Hypothesis

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The influence of a dysregulated metabolic intrauterine environment on infant neurodevelopment has gained interest over the years. There is growing evidence for the role of maternal diabetes before and during pregnancy in the pathogenesis of neurodevelopmental disorders such as autism spectrum disorder (ASD), attention deficit hyperactive disorder (ADHD), internalisation, externalisation symptoms, gross and fine motor development.^(1,2,3) However, studies examining associations of gestational diabetes mellitus (GDM) with neurodevelopmental health outcomes such as ASD and ADHD have reported inconsistent results. More studies based on larger sample sizes, harmonised information on GDM, ASD and ADHD diagnosis, longer offspring follow-up time are required to confirm an association between maternal diabetes with childhood neurodevelopment health outcomes. Our primary aim was to study the association of diabetes during pregnancy on various aspects of child cognitive and behavioural disorders such as ASD, ADHD, internalisation, externalisation symptoms, gross and fine motor development at different ages. We used harmonised data from ten cohorts (a maximum of 257,778 mother–child dyads) from cohorts across Europe and Australasia for children between 3 and 13 years old. Harmonised GDM data (yes or no) was available for all participants. We used child cognitive and behavioural outcomes at four age periods (dependent on available information of each cohort) (i) 3 years, (ii) 4–6 years, (iii) 7–10 years and (iv) 3 years. Associations were examined through the DataSHIELD platform using adjusted logistic regression models, fitted separately for each cohort and pooled via one-stage meta-analysis. The prevalence of GDM among the cohorts ranged from 0.7% to 8.0%. GDM was associated with ASD ($\beta = 6.92$, 95% CI [1.17, 12.68], $p = 0.02$) and ADHD ($\beta = 3.41$, 95% CI [1.85, 4.98], $p < 0.001$) problems in children 4–6. Similar, GDM was also associated with ASD ($\beta = 4.42$, 95% CI [0.11, 8.72], $p = 0.04$) and ADHD ($\beta = 3.52$, 95% CI [1.41, 5.64], $p = 0.001$) problems for 7–10 years. After adjustment for birth weight, parity, plurality, pre-pregnancy weight and EUSILC household income, GDM was still associated with ADHD in children 4–6 years ($\beta = 1.73$, 95% CI [−0.21, 3.67], $p = 0.001$) and 7–10 years ($\beta = 2.41$, 95% CI [−0.07, 4.75], $p = 0.04$). However, the associations between GDM and ASD were no longer apparent after adjustment. GDM was also positively associated with gross and fine motor development at a younger but not older age. Our findings suggest that maternal diabetes in pregnancy may increase neurodevelopment in young children (4–10 years). But the evidence for association in older children was weak. Maternal socioeconomic positions such as maternal education and household income may influence outcomes, and mediating variables should be further investigated.

References

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