EDITORIAL

Pre-eclampsia may raise risk of autism spectrum disorder

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MATERNAL PRE-ECLAMPSIA IS ASSOCIATED WITH AN INCREASED RISK OF AUTISM SPECTRUM DISORDER (ASD) in offspring, a meta-analysis has found.[1]

The investigators searched PubMed, Embase and PsycINFO databases for eligible studies. Ten studies met the inclusion criteria, six were case control and four cohort studies. Sample sizes ranged from 867 to 377,708 participants. Three studies were carried out in the USA, the others in Australia, Canada and Scandinavia.

> **'Compared with unexposed offspring children who were exposed to pre-eclampsia in utero were 32% more likely to develop autism spectrum disorder'**

Data were obtained from medical records, clinical databases and national registers. Only one of the studies used a standard clinical definition of pre-eclampsia; most of the studies adopted the ICD diagnostic criteria for ASD. There was no significant heterogeneity or evidence of publication bias.

Seven of the studies found a positive association between pre-eclampsia and ASD, the others a null association. Compared with unexposed offspring, children who were exposed to pre-eclampsia in utero were 32% more likely to develop ASD; relative risk (RR) 1.32 (95% CI: 1.20-1.45). Sensitivity analysis (repeating the meta-analysis, each time omitting one of the studies) did not significantly change the result.

A causal relationship between pre-eclampsia and ASD, mediated by fetal hypoxia, oxidative stress or maternal systemic inflammation, is certainly plausible.[2] ASD has been linked to low birthweight, prematurity and birth asphyxia, all of which may result from pre-eclampsia.

However, it is equally possible that the association was due to confounding by risk factors common to both conditions, including advanced maternal age, obesity, diabetes and gestational diabetes (prior to 26 weeks).[3] It is unfortunate that the included studies did not consistently adjust for these and other potential confounders.

NICE recommends that, when considering a referral to the autism team, account should be taken of factors associated with an increased prevalence of autism. These include: a sibling with autism, congenital abnormalities of the central nervous system including cerebral palsy, a gestational age less than 35 weeks, parental schizophrenia and maternal use of valproate in pregnancy.[4] Maternal pre-eclampsia should now be added to this list, together with maternal obesity, diabetes and gestational diabetes.

The study authors conclude: 'This study suggests that early screening for ASD in offspring of women with pre-eclampsia may be warranted and, future studies should assess the effect of early screening and treatment of pre-eclampsia on the prevention of ASD in offspring.'

However, given an ASD prevalence of 1% in the UK,[5] the absolute risk is only increased by 3 cases per 1,000 and personally I do not feel this is sufficient to justify screening.

The main lesson from this study is to take a detailed obstetric history when considering the possibility of autism.

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