

Associations of Maternal Antidepressant Use During the First Trimester of Pregnancy with Preterm Birth, Small for Gestational Age, Autism Spectrum Disorder, and Attention-Deficit/Hyperactivity Disorder in Offspring.

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ABSTRACT

IMPORTANCE:

Prenatal antidepressant exposure has been associated with adverse outcomes. Previous studies, however, may not have adequately accounted for confounding.

OBJECTIVE:

To evaluate alternative hypotheses for associations between first-trimester antidepressant exposure and birth and neurodevelopmental problems.

DESIGN, SETTING, AND PARTICIPANTS:

This retrospective cohort study included Swedish offspring born between 1996 and 2012 and followed up through 2013 or censored by death or emigration. Analyses controlling for pregnancy, maternal and paternal covariates, as well as sibling comparisons, the timing of exposure comparisons, and paternal comparisons, were used to examine the associations.

EXPOSURES:

Maternal self-reported first-trimester antidepressant use and first-trimester antidepressant dispensations.

MAIN OUTCOMES AND MEASURES:

Preterm birth (<37 gestational weeks), small for gestational age (birth weight <2 SDs below the mean for gestational age), and first inpatient or outpatient clinical diagnosis of autism spectrum disorder and attention-deficit/hyperactivity disorder in offspring.

RESULTS:

Among 1 580 629 offspring (mean gestational age, 279 days; 48.6% female; 1.4% [n = 22 544] with maternal first-trimester self-reported antidepressant use) born to 943 776 mothers (mean age at childbirth, 30 years), 6.98% of exposed vs 4.78% of unexposed offspring were preterm, 2.54% of exposed vs 2.19% of unexposed were small for gestational age, 5.28% of exposed vs 2.14% of unexposed were diagnosed with autism spectrum disorder by age 15 years, and 12.63% of exposed vs 5.46% of unexposed were diagnosed with attention-deficit/hyperactivity disorder by age 15 years. At the population level, first-trimester exposure was associated with all outcomes compared with unexposed offspring (preterm birth odds ratio [OR], 1.47 [95% CI, 1.40-1.55]; small for gestational age OR, 1.15 [95% CI, 1.06-1.25]; autism spectrum disorder hazard ratio [HR], 2.02 [95% CI, 1.80-2.26]; attention-deficit/hyperactivity disorder HR, 2.21 [95% CI, 2.04-2.39]). However, in models that compared siblings while adjusting for pregnancy, maternal, and paternal traits, first-trimester antidepressant exposure was associated with preterm birth (OR, 1.34 [95% CI, 1.18-1.52]) but not with small for gestational age (OR, 1.01 [95% CI, 0.81-1.25]), autism spectrum disorder (HR, 0.83 [95% CI, 0.62-1.13]), or attention-deficit/hyperactivity disorder (HR, 0.99 [95% CI, 0.79-1.25]). Results from analyses assessing associations with maternal dispensations before pregnancy and with paternal first-trimester dispensations were consistent with findings from the sibling comparisons.

CONCLUSIONS AND RELEVANCE:

Among offspring born in Sweden, after accounting for confounding factors, first-trimester exposure to antidepressants, compared with no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder.