

## Association of Severe Preeclampsia with Offspring Neurodevelopmental and Psychiatric Disorders: A Finnish Population-Based Cohort Study

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**Abstract :** Background: Prenatal exposure to preeclampsia has been associated with an increased risk of offspring attention-deficit/hyperactivity disorders (ADHD), autism spectrum disorder (ASD), and intellectual disability. However, little is known about the association between prenatal exposure to severe preeclampsia and neurodevelopmental and psychiatric disorders in offspring. Objective: This study aimed to assess the risk of maternal preeclampsia combined with perinatal problems, specifically low birth weight and prematurity, on offspring neuropsychiatric disorders. Methods: All singleton live births in Finland between 1996 and 2014 (n=1 012 723) were followed up in nation-wide registries until 2018. Main exposures included pre-eclampsia, small for gestational age, and delivery before 34 gestational weeks. Offspring neurodevelopmental and psychiatric disorders (ICD-10 codes) were examined as outcomes variables. Offspring birth year, sex, maternal age at delivery, parity, marital status at birth, mother's country of birth, maternal smoking, maternal gestational diabetes, maternal use of psychotropic medication during pregnancy, and maternal systemic inflammatory diseases were used as covariates. Risks for neurodevelopmental and psychiatric disorders were estimated using Cox proportional hazards modeling. Results: Of the 1 012 723 offspring, 25 901 (2.6%) were exposed to preeclampsia, and 93 281 (9.2%) were diagnosed with a neuropsychiatric disorder. Compared to births unexposed to preeclampsia, small for gestational age or delivery before 34 gestational weeks, those exposed to preeclampsia only had a 21% increase in the likelihood of any neuropsychiatric disorders after adjusting for potential confounding (adjusted HR=1.21, 95% CI: 1.15-1.26), while exposure to preeclampsia combined with small for gestational age or delivery before 34 gestational weeks had a more than twofold increased risk of having a child with neuropsychiatric disorders (adjusted HR=2.16, 95% CI: 2.02-2.32). The adjusted HR for neuropsychiatric disorders in offspring with small for gestational age or delivery before 34 gestational weeks only was 1.79 (95% CI: 1.73-1.83). In addition, the risk estimate in offspring exposed to both preeclampsia and perinatal problems was greater than those only exposed to preeclampsia for having personality disorders (adjusted HR=1.66; 95% CI: 1.07-2.57), intellectual disabilities (adjusted HR=3.47; 95% CI: 2.86-4.22), specific developmental disorders (adjusted HR=2.91; 95% CI: 2.69-3.15), ASD (adjusted HR=1.75; 95% CI: 1.42-2.17), ADHD and conduct disorders (adjusted HR=2.00; 95%CI: 1.76-2.27), and other behavioral and emotional disorders (adjusted HR=2.09; 95% CI: 1.84-2.37). Conclusion: In utero exposure to severe preeclampsia increased the risk of several neurodevelopmental and psychiatric disorders in offspring. Our findings are relevant to women with hypertensive disorders with regard to pregnancy consultation and management and may yield effective clues for the prevention of neurodevelopmental and psychiatric disorders in childhood.

**Keywords :** low birth weight, neurodevelopmental disorders, preeclampsia, prematurity, psychiatric disorders

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