

# Preeclampsia May Put Adult Offspring at Risk of Stroke

BY HEIDI SPLETE  
Senior Writer

WASHINGTON — A maternal history of preeclampsia may identify adults who are at increased risk for stroke.

Adults whose mothers had severe preeclampsia were almost twice as likely to have strokes, compared with adults whose mothers didn't have preeclampsia, based on data from more than 6,000 singleton pregnancies in Finland.

This study is one of the first to examine the long-term health risks of the offspring of women who had preeclampsia, Dr. Eero Kajantie said at the annual congress of the International Society for the Study of Hypertension in Pregnancy. "We know surprisingly little about which pregnancy conditions are associated with increased risk for coronary heart disease and stroke" among offspring.

Previous studies have shown that these women are at increased risk for coronary heart disease and stroke later in life. Also, their children are prone to high blood pressure during childhood, said Dr. Kajantie of the National Public Health Institute in Helsinki.

Dr. Kajantie and his colleagues based their conclusion on a review of data from

6,410 members of the Helsinki Birth Cohort, who were born as singletons between 1934 and 1944.

Overall, 284 pregnancies (4.4%) were complicated by preeclampsia and 1,592 (24.8%) met criteria for hypertension without proteinuria. Among the children of these pregnancies, 464 (7.2%) had a diagnosis of coronary heart disease and 272 (4.2%) had a diagnosis of stroke. Diagnoses of CHD and stroke were collected from national hospital discharge records and death registries.

The risk of stroke was almost twice as likely in the 164 adults whose mothers had severe preeclampsia (hazard ratio, 1.7), after the researchers controlled for sex, low birth weight, and gestational age.

The researchers also examined hypertension without proteinuria as an outcome. They found that hypertension was a significant predictor of stroke, but that it was not a significant predictor of CHD.

"People born from pregnancies complicated by preeclampsia are at increased risk of stroke and hypertension," Dr. Kajantie said. "We were unable to show any association with CHD, although we are unable to exclude a small increase."

Dr. Kajantie had no financial conflicts to disclose. ■

# Hypertension in Pregnancy Ups Risk for Later HT, Stroke

BY HEIDI SPLETE  
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WASHINGTON — Women who had hypertension during pregnancy are at increased risk for hypertension and stroke after 40 years of age.

Follow-up data from more than 4,000 women suggest providers should ask patients about a history of hypertension in pregnancy and note the increased risk of hypertension and stroke in those with such a history, said Dr. Vesna D. Garovic of the department of nephrology and hypertension at the Mayo Clinic in Rochester, Minn.

The current findings support previous research, but earlier studies have been small and registry-based, with limited follow-up, Dr. Garovic said at the annual congress of the International Society for the Study of Hypertension in Pregnancy.

Dr. Garovic and her colleagues reviewed data from 4,782 women in the Family Blood Pressure Program, a multicenter genetic study of high blood pressure and related conditions, to assess the role of hypertension in pregnancy as a risk factor for subsequent stroke and coronary heart disease.

The women were divided into three categories: those with no history of a full-term pregnancy, those with no history of hypertension in pregnancy, and those with a history of hypertension in at least one pregnancy. The women were also asked about other risk factors, including a family history of hypertension

and a history of smoking, she explained.

The investigators tracked hypertension and related conditions after the women reached age 40 years. Overall, those with a history of hypertension in pregnancy had a significantly increased risk for hypertension, coronary heart disease (CHD), and stroke, compared with those who were not hypertensive in pregnancy.

After controlling for cardiovascular factors including race, family history of CVD, diabetes, dyslipidemia, and smoking, only the risk for hypertension later in life was significantly higher (hazard ratio, 1.88). After controlling for risk factors for stroke, including subsequent hypertension, the stroke risk was significantly increased (HR 2.10), but the CHD risk was not.

Women with a history of hypertension in pregnancy also developed hypertension at a younger age than did those who weren't hypertensive in pregnancy. Of 643 women with a history of hypertension in pregnancy, 50% were hypertensive by age 53 years.

"You can postulate that [they] have some underlying increased risk," but hypertension in pregnancy may cause changes that contribute to an increased risk of future cardiovascular disease, she said, adding that the study was limited by selection bias and the use of self-reports.

The mechanism of action that connects hypertension in pregnancy to subsequent disease risk remains unknown.

Dr. Garovic stated that she had no conflicts of interest to disclose. ■

## DRUGS, PREGNANCY, AND LACTATION

### Pulmonary Hypertension and SSRIs

Over the last several years, the reproductive safety of selective serotonin reuptake inhibitors (SSRIs) has been the focus of continual interest and concern, with data from several studies informing the question of relative risks of fetal exposure to these medicines. Two recent analyses from large birth defects surveillance programs suggest that the risk for major malformations associated with first-trimester exposure to SSRIs is extremely small (*N. Engl. J. Med.* 2007;356:2684-92, 2675-83).

On the basis of the results of other studies that are particularly consistent, there now appears to be a consensus that late-trimester exposure to SSRIs is associated with an increased risk for symptoms broadly described as "poor neonatal adaptation" including: tremulousness, jitteriness, and myoclonus. These symptoms tend to be transient, and their clinical relevance appears to be limited—because infants born with these symptoms typically do not require any particular clinical intervention.

More recently, an increased risk of a far more serious condition, persistent pulmonary hypertension of the newborn (PPHN), has been associated with exposure to SSRIs late in pregnancy. The first study to describe this association, derived from a case-control study using data from a birth defects database, reported that in utero SSRI exposure after 20 weeks' gestation was associated with an increased risk of PPHN (about sixfold higher), with an absolute risk approaching 1% (*N. Engl. J. Med.* 2006;354:579-87). When it was published, the study elicited great concern among providers and patients; the Food and Drug Administration also suggested inclusion of the finding in the labels of SSRIs.

Factors driving the risk for PPHN have been studied extensively and were the focus of a case-control study of the same birth defects database published last year that found a strong association between PPHN and several common prenatal and perinatal factors, including cesarean delivery, high maternal BMI, being African American or Asian, and being large for gestational age (*Pediatrics* 2007;120:e272-e82). Though extensive discussion was not given in that article about the relative contributions of these common factors to risk for PPHN, compared with SSRI exposure late in pregnancy, the data suggest that large BMI and cesarean delivery, for example, drive PPHN to a far greater extent than SSRI exposure.

The association between SSRI exposure during pregnancy and PPHN was again addressed recently in a case-control study using data from the Swedish Medical Birth Register of over 800,000

infants born between 1997 and 2005; 506 infants had a discharge diagnosis of PPHN. Across a wide variety of SSRIs to which women had been exposed, the risk of PPHN associated with maternal use of an SSRI among babies born after 34 weeks' gestation was increased by 2.4, after adjusting for other risk factors (*Pharmacoepidemiol. Drug Saf.* 2008;17:801-6). This finding was among the women who reported using an SSRI when interviewed early in pregnancy, before the end of the first trimester—a marginally statistically significant increase. These results are consistent with the results of the 2006 study, but suggest a more attenuated risk and might explain why physicians with patients treated with an SSRI during pregnancy rarely see this condition.

The results may be considered somewhat reassuring because they suggest that even if there is an increased risk, the increase is small. Considering the prevalence of SSRI use during pregnancy—as high as 6%-8%, according to several recent studies—PPHN presumably would be seen more often if the risk were as high as 1%. (On the other hand, it is common to hear about neonatal adaptation symptoms in babies who have been exposed in late pregnancy to SSRIs, where estimates of the prevalence of such symptoms are 25%-30%.)

One of the obvious advantages of the Swedish study was that the information about SSRI use was obtained prospectively and did not rely on retrospective recall, as was the case in the 2006 study. But no study is perfect and, in the Swedish study, the investigators were not able to distinguish between early and late exposure. Late exposure was extrapolated by assuming that women on the drug early in pregnancy were also on the drug late in pregnancy. That is not a trivial limitation, because of evidence indicating that is not uncommon for women who are on an antidepressant in early pregnancy to discontinue treatment after either documentation of pregnancy or later in pregnancy.

The results of new studies sometimes either refute current associations or suggest greater or lesser associations. Ultimately, providers and their patients make collaborative decisions, and treatment will be tailored to match the clinical situation using the best available data possible.

DR. COHEN directs the perinatal psychiatry program at Massachusetts General Hospital, Boston, which provides information about pregnancy and mental health at [www.womensmentalhealth.org](http://www.womensmentalhealth.org). He also is a consultant to manufacturers of antidepressants, including SSRIs.



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