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High levels of hormones during pregnancy associated with higher risk for HR-negative breast cancer

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Increased concentrations of the pregnancy hormones estradiol and progesterone were associated with an increased risk for hormone receptor-negative breast cancer diagnosed before age 50, according to the results of a nested case-control study presented at the 11th Annual AACR International Conference on Frontiers in Cancer Prevention Research, held here Oct. 16-19, 2012.

Annekatrin Lukanova, M.D., Ph.D., associate professor at the German Cancer Research Center in Heidelberg, Germany, and colleagues examined the effects of hormonal exposure during early pregnancy and its possible association with risk for maternal breast cancer.

"Pregnancy influences maternal risk for breast cancer, but the association is complex and the biological mechanisms underlying the associations are unknown," Lukanova said. "Understanding the mechanisms underlying the protective effect of childbearing on cancer risk can form the basis for primary prevention of breast cancer."

Lukanova and colleagues used the Northern Sweden Maternity cohort to conduct a nested case-control study of 417 controls and 223 women who had donated blood samples during their first trimester of pregnancy and were later diagnosed with breast cancer. About three quarters of the breast cancer cases were hormone receptor (HR)-positive.

The researchers examined two groups of hormones: The first group included estradiol, estrone and progesterone, the concentrations of which increase substantially with pregnancy progression. The second group included testosterone and insulin growth factor-1 (IGF-1). During early pregnancy, concentrations of testosterone and IGF-1 are largely similar to prepregnancy concentrations.

"We found that circulating concentrations of IGF-1 and testosterone are directly associated with risk for HR-positive breast cancer, in line with studies in nonpregnant women," Lukanova said.

Results indicated a heightened risk for HR-negative breast cancer diagnosed before 50 years of age with increased levels of estradiol and progesterone.

Lukanova noted that this study was small, that the hormones were measured during the first trimester of pregnancy only, and that further and larger studies will be necessary to characterize the association of pregnancy hormones with risk for hormone-defined maternal breast cancer.

More information: B75 Pregnancy hormones and maternal risk of hormone receptor-defined breast cancer. Annekatrin Lukanova et al.

Abstract
Introduction: Hormonal exposure during pregnancy is believed to be associated with subsequent maternal risk of breast cancer, but so far limited epidemiological data are available.

Study design: A case-control study (223 cases and 417 controls) was nested within the Northern Sweden Maternity Cohort to explore the associations between pregnancy concentrations of sex steroid hormones and insulin-like growth factor I (IGF-I) with maternal risk of breast

cancer by hormone receptor (HR) expression of the tumors. The study included women who had donated a blood sample during the first trimester of their first full-term pregnancy. Most cases had HR-positive disease: 171 (77%) estrogen receptor-positive (ER+), 157 (70%) progesterone receptor-positive (PR+) and 152 (68%) ER+/PR+ tumors. Estradiol, estrone, progesterone and testosterone were measured by high-performance liquid chromatography tandem mass spectrometry. Sex hormone-binding globulin (SHBG) and insulin-like growth factor I (IGF-I) were measured by immunoassays. For each hormone, the difference (residual) between the actual assay value for each subject and the estimated mean determined for the day of gestation when the sample was drawn was computed by local linear regression. Conditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI).

Results: For HR-positive tumors, a significant direct association was observed with circulating concentrations of testosterone (e.g. OR for ER+ in the top versus bottom tertile of 1.8 (1.1-3.0), p