Hormone Concentrations during Pregnancy and Maternal Risk of Epithelial Ovarian Cancer

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie doktorsexamen framläggs till offentligt förvar i Betula, By 6M, Norrlands Universitetssjukhus, fredagen den 22 maj, kl. 09:00.
Avhandlingen kommer att försvaras på engelska.

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Background: The aim of this thesis was to study the relationship of pre-diagnostic circulating concentrations of sex steroid hormones (androgens, estradiol, 17-hydroxyprogesterone, and progesterone), growth factors (insulin-like growth factor-I (IGF-I), placental growth hormone (GH)), sex hormone binding globulin (SHBG), and anti-Müllerian hormone (AMH) with risk of epithelial ovarian cancer (EOC) overall, and by tumor invasiveness and histology. A longitudinal study was used to assess patterns of hormonal changes during a single pregnancy, and in two consecutive pregnancies.

Materials & Methods: A case-control study was nested within the Finnish Maternity Cohort and the Northern Sweden Maternity Cohort. A total of 1,052 EOC cases were identified through linkages with the cancer registries in both countries. For each case, 2-3 controls were selected. Cases and controls were matched on cohort, age and date at blood draw, as well as for parity at blood draw and at diagnosis (n=2,695). Odds ratios (OR) and corresponding 95% confidence intervals [CI] were estimated using conditional logistic regression. The longitudinal study was based on 71 pregnant Finnish women, who donated blood samples in each trimester of pregnancy.

Results: Higher androgen concentrations were associated with an increased risk of overall EOC (e.g., testosterone OR T3 vs. T1: 1.56 [1.30-1.87], p_{trend}<0.0001), while the risk of endometrioid tumors increased with higher estradiol concentrations (OR T3 vs. T1: 2.76 [1.04-7.33], p_{trend}=0.03). Higher IGF-I was associated with a non-significant decrease in risk for invasive (OR T3 vs. T1: 0.79 [0.62-1.02], p_{trend}=0.07) and endometrioid tumors (OR T3 vs. T1: 0.55 [0.28-1.07], p_{trend}=0.07). The inverse association between IGF-I levels and risk of invasive EOC was stronger in analyses limited to women aged <55 years at diagnosis (OR T3 vs. T1: 0.74 [0.57-0.96], p_{trend}=0.03). No associations were observed between pre-diagnostic progesterone, SHBG, placental GH, and AMH with EOC risk overall, or by tumor invasiveness and histology. The longitudinal study showed that hormone concentrations were more strongly correlated between consecutive trimesters of a pregnancy than between the 1st and 3rd trimesters. Further, 3rd trimester hormone concentrations can be estimated from 1st or 2nd trimester measurements.

Conclusion: Higher pre-diagnostic androgens, estradiol, and IGF-I are associated with EOC risk, and associations differ by tumor invasiveness and histology.

Keywords: epithelial ovarian cancer; sex steroid hormones; IGF-I; placental GH; AMH; pregnancy; prospective study.