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Determinants of maternal hair cortisol concentrations at delivery reflecting the last trimester of pregnancy

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Summary Hair cortisol concentrations (HCC) are emerging as a promising marker of chronic psychosocial stress. However, limited information on relevant correlates of this biomarker in late pregnancy is available. In the Ulm SPATZ Health Study mothers were recruited between 04/2012 and 05/2013 shortly after delivery in the University Medical Center Ulm, Germany. Cortisol concentrations of $N = 768$ participants were determined by HPLC—MS/MS in the scalp-near 3 cm of maternal hair reflecting stress exposure over the preceding three months. Sociodemographic characteristics, pregnancy-related variables and comorbidities were assessed. We conducted bivariate and multiple linear regression analyses using log transformed HCC. In bivariate analyses, significantly higher cortisol concentrations were found in obese compared to normal weight ($b = 0.32$, $p < 0.001$) and smoking as opposed to non-smoking mothers ($b = 0.34$, $p = 0.002$). Conversely, primary C-section was associated with lower HCC compared to spontaneous delivery. Besides, a strong impact of season of delivery with significantly higher HCC in summer and autumn as opposed to winter (both bs = 0.58, $p < 0.001$) was found. Further determinants of HCC were maternal education, number of persons in the household, premature delivery and hair characteristics. In a mutually adjusted model, all but education, multiple jobholding, hair characteristics and premature delivery remained statistically significant.

Maternal hair cortisol in the last trimester of pregnancy is determined by many factors. Delivery mode, body mass index and season of delivery should be considered when investigating the association between HCC and further outcomes in mothers shortly after delivery.

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1. Introduction

Maternal psychosocial distress during pregnancy is associated with poor pregnancy outcomes like low gestational age, birth weight or body length, as well as a high risk of miscarriage and may affect offspring's morbidity in later life (Beydoun and Saftlas, 2008; Graignic-Philippe et al., 2014).

Among others, one potential mechanism linking maternal psychosocial distress (in the following referred to as stress) to infant health is the hypothalamus—pituitary—adrenal (HPA) axis with its final effector, cortisol. However, cortisol secretion is characterized by a considerable degree of intra- and interindividual variability due to specific circadian patterns. Beyond that, high susceptibility to situational characteristics (Hellhammer et al., 2007; Kudielka et al., 2009; Stalder and Kirschbaum, 2012) makes measuring basal cortisol secretion challenging.

In this context, the analysis of steroids in hair is an important methodological development. Long periods of stress were associated with increased hair cortisol concentrations (HCC) in animals (Davenport et al., 2006) and humans (review: Staufenbiel et al., 2013; original articles: O'Brien et al., 2012; Henley et al., 2013; Stalder et al., 2014). Furthermore, a range of studies have now provided direct and indirect support for the validity of HCC as measures of long-term cortisol secretion (Thomson et al., 2010; Stalder and Kirschbaum, 2012).

Only recently, potentially influencing factors on HCC have been studied (Dettenborn et al., 2012; Feller et al., 2014) and reviewed (Wosu et al., 2013). Socioeconomic aspects, age, race, psychiatric symptoms, and hair characteristics have been identified as important factors associated with HCC. However, results are still controversial. Furthermore, late pregnancy, identified as a state of elevated cortisol level (Kirschbaum et al., 2009; D'Anna-Hernandez et al., 2011), may constitute a highly specific period of cortisol secretion, possibly differing from other stages of life. Research on HCC in pregnant women is limited to few previous studies having rather small sample sizes (Kalra et al., 2007; Kirschbaum et al., 2009; Kramer et al., 2009; D'Anna-Hernandez et al., 2011) and lacking details on potential predictors of HCC. Therefore, the purpose of the present study was to examine potential determinants of HCC as a measure of HPA axis activity in a large number of women consecutively recruited shortly after delivery.

2. Material and methods

2.1. Study design and study population

We analyzed data from a population-based, prospective birth cohort study, the Ulm SPATZ Health Study, initiated at Ulm University, Germany. All women who came to the University Medical Center Ulm between 04/2012 and 05/2013 for the delivery of their baby were asked to participate (overall response 49%). Exclusion criteria were: inadequate German language skills, outpatient childbirth, maternal age less than 18 years, postpartal transfer of mother or child to an intensive care unit, or stillbirth. Participation was voluntary and informed consent was obtained for each case. The study was approved by the ethics board of Ulm University (no. 311/11).

2.1.1. Collection and laboratory measurement of hair cortisol

Hair was collected from the posterior vertex region of the maternal head at the time of delivery (in median 1.5 days after delivery, 25th percentile: 1.0, 75th percentile: 2.0). Two strands of hair were cut as close to the scalp as possible using scissors. Hair samples were wrapped in aluminum foil, the scalp end was marked and samples were stored at room temperature. Strands of 3 cm adjacent to the scalp were analyzed. Given an average hair growth rate of 1 cm/month (Wennig, 2000), the examination of a 3 cm hair segment allowed to assess cumulative HCC over a period of three months, i.e., the last trimester of pregnancy in our study. Hair cortisol was extracted following a protocol described elsewhere (Gao et al., 2013).

Briefly, samples were washed in 2.5 mL isopropanol for 3 min, and cortisol was extracted from 7.5 mg of whole, nonpulverised hair using 1.6 mL methanol in the presence of 20 μL cortisol-d_4 as internal standard for 18 hours at room temperature. Samples were spun in a centrifuge at 15,200 $\times$ g relative centrifugal force for 2 min and 1 mL of the clear supernatant was transferred into a new 2 mL tube. The alcohol was evaporated at 65 °C under a constant stream of nitrogen and reconstituted with 150 μL double-distilled water. Samples were analyzed by a Shimadzu HPLC-tandem mass spectrometry system (Shimadzu, Canby, OR) coupled to an ABSciex API 5000 Turbo-ion-spray triple quadrupole tandem mass spectrometer (AB Sciex, Foster City, CA) with purification by on-line solid-phase extraction. This method has been shown to achieve excellent sensitivity, specificity and reliability (intra and inter-assay CVs between 3.7 and 8.8%) (Gao et al., 2013). All measures were done in blinded fashion.

2.1.2. Sociodemographics, familial characteristics, lifestyle factors and hair characteristics

Factors potentially influencing HCC were assessed by a self-administered standardized questionnaire handed out to the mother shortly after the delivery: Maternal nationality (derived from nationality and country of birth), maternal education ($\leq$9 years, 10—11 years, >11 years of school education), maternal age at delivery in years, type of maternal employment before maternity leave (one employment or self-employed, multiple jobholding, no paid employment), and persons living in the household including the newborn (continuously and in the following categories (2, 3—4, >4 persons)). Furthermore, the mother was asked if she had been unemployed (yes/no) at the time of delivery. Hair characteristics assessed via questionnaire included information on normal frequency of hair washing per week (number), natural hair color (very blond or blond, brown, red, and black; the latter two grouped due to the small sample size for red hair) and hair bleaching at present (yes/no).

2.1.3. Delivery outcomes and delivery-related factors

Season of delivery (December—February, March—May, June—August, September—November), mode of delivery (spontaneous vaginal, primary C-section, secondary