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ORIGINAL ARTICLE

Maternal Stress in Gestation: Birth Outcomes and Stress-Related Hormone Response of the Neonates

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neonate neurobehavioral development;
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Background: Relatively few studies have been made on neurobehavioral outcomes of prenatal maternal stress during the newborn period, and little research has focused on umbilical cord stress hormones including cortisol, adrenocorticotropic hormone (ACTH), norepinephrine, and epinephrine. Our objective was to investigate the effects of prenatal maternal life stressors on neonatal birth outcomes, neurobehavioral development, and stress-related hormones levels.

Methods: Participants were 142 mothers and their infants; 71 were selected as the prenatal life stressor exposed group and 71 as the control group matched on maternal age, gestational week, delivery type, socioeconomic and education status, and newborns' sex. Maternal life stressors during pregnancy were determined using the Life Events Scale for Pregnant Women. Neonatal neurobehavioral development was assessed with the Neonatal Behavioral Neurological Assessment. Umbilical cord plasma stress-related hormones, including ACTH, cortisol, norepinephrine, and epinephrine were measured using an enzyme-linked immunosorbent assay.

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Results: In the prenatal life stressors exposed group, newborns had significantly lower birth weight, smaller head circumference ($p < 0.01$, $p < 0.01$, respectively). Scores of Neonatal Behavioral Neurological Assessment were significantly reduced ($p < 0.001$). Cord plasma ACTH, norepinephrine, and epinephrine levels were significantly increased ($p < 0.001$), but cortisol levels were reduced ($p < 0.001$).
Conclusion: Prenatal maternal stress may negatively affect fetal birth outcomes, neurobehavioral development and affect neonates' cord plasma ACTH, cortisol, norepinephrine, and epinephrine.

1. Introduction

Findings indicate that the human fetus is exquisitely sensitive to physiological and psychological maternal stress, and prenatal stress can be measured with psychometric instruments.[1] It has been proposed that prenatal maternal stress is linked to low birth weight (BW),[2] lower BW, and smaller head circumference (HC).[3] Studies also show that chronic prenatal maternal stress impairs fetal neurobehavioral development.[4] Sandman et al[5] found that prenatal maternal stress disrupted cognitive performance during infancy and decreased brain volume in areas associated with learning and memory in 6- to 8-year-old children.

The hypothalamic—pituitary—adrenal (HPA) axis is one of the major systems involved in stress response and regulation.[6] Data from a wide range of studies indicate that prenatal maternal stress is associated with elevated maternal cortisol levels during pregnancy, which can pass through the placenta in sufficient concentrations and increase fetal cortisol concentration.[7] However, Nierop et al[8] concluded that pregnancy in women did not result in a restraint of the HPA axis to psychosocial stress. In addition, Entringer et al[9] retrospectively identified pregnant women who had been exposed to a severe life event and found the young adult offspring of the exposed group had a lower plasma cortisol but higher adrenocorticotropic hormone (ACTH) stress response. Therefore, cortisol response to stress events across studies is inconsistent.

The sympathetic—adrenal—medullary system (SAM), another neuroendocrine system, is known to be highly pliable and susceptible to the influence of environmental factors during development. Various studies report neonatal plasma norepinephrine (NE) and epinephrine (E) levels significantly increase with response to stress.[10] A direct relationship between prenatal maternal stress and low birth weight, lower BW, and smaller HC may be related to the release of catecholamines, resulting in placental hypoperfusion and consequent restriction of oxygen and nutrients to the fetus, leading to fetal growth impairment.[11]

Relatively few studies have been conducted into neurobehavioral outcomes of prenatal maternal stress during the newborn period, and little research has focused on umbilical cord stress hormones. Furthermore, due to interrelation between the HPA axis and the SAM, examination of both these systems has an increased possibility of providing valuable information about neuroendocrine changes.

In the present research, our objectives were to assess prenatal maternal stress on newborns' BW and HC, neurobehavioral development, to analyze umbilical cord plasma ACTH, cortisol, NE, and E levels, and to explore whether prenatal maternal stress induce alterations of both hormones, birth outcomes, and neurobehavioral outcomes of newborns.

2. Methods

2.1. Study design and participants

In total, 327 neonates and their mothers were recruited from the Department of Gynecology and Obstetrics of the First Affiliated Hospital, Medical School of Xi'an Jiaotong University, Xi'an, China, from February to August 2010. The following inclusion criteria were applied: (1) mother aged 20—35 years; (2) first singleton pregnancy; (3) birth with no *intrapartum* complications; (4) gestation at birth 37—40 weeks and the baby developed normally; (5) Apgar score >7 at the 1st minute, 5th minute, and 10th minute after birth; (6) babies' umbilical cord venous blood were collected; and (7) had a higher score (≥375) of Life Events Scale for Pregnant Woman (LESPW). Mothers and their neonates were excluded from the study if: (1) the mother used drugs or medication with risks for the fetus; (2) the mother was a smoker or drinker; (3) the mother developed any disease such as hypertension of pregnancy, gestational diabetes mellitus, hyperthyroidism, intrahepatic cholestasis of pregnancy, tumor, hysteromyoma, or abnormal pregnancy complications such as placental abruption or placenta previa; (4) the mother had abnormal gestation or birth history, such as habitual abortion or stillbirth; (5) the mother could not cooperate with us in the survey; or (6) neonates developed congenital malformation, congenital diseases, asphyxia, or birth trauma. Of the 327 mothers who had a higher score (LESPW score ≥ 375), 38 women accepted tocolytic therapy, 14 bore twins and five had stillbirths, six women had preterm delivery, and 159 were excluded because the cord blood was not collected. Of the remaining 105 cases, 27 who had pregnancy-induced hypertension and seven who had intrahepatic cholestasis