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# Maternal Nutritional and Water Homeostasis as a Presage of Fetal Birth Weight

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**Abstract**

Birth weight is a key determinant of perinatal outcomes which affect physical development and metabolic function. In this study, we evaluated the potential role of maternal body composition and nutritional status in programing fetal birth weight. This was a longitudinal study that included 29 pregnant women and their full-term newborns. Maternal dietary energy and fluid intake and body adipose tissue were assessed. In addition, we measured the serum content of copeptin, aldosterone, and angiotensin II in maternal and umbilical cord blood. The measurements were done across the three trimesters of pregnancy, on average, at 11.6 weeks, 18.3 weeks, and 30.2 weeks. Each newborn's birth weight was determined at the percentile line, using the World Health Organization (WHO) standards based on the gestational age, gender, and weight. We found no appreciable relation of fetal birth weight to the maternal dietary and fluid intakes, and the content of angiotensin II, aldosterone, or copeptin. However, birth weight correlated with increases in body adipose tissue in early pregnancy stages. Further, birth weight correlated positively with copeptin and adversely with angiotensin II in cord blood. We conclude that the present findings may be helpful in the assessment of a critical level of body adipose tissue in women of child-bearing age, above which the potential risk of macrosomia appears. The female population of child-bearing age needs a continual update on the nutritional knowledge to prevent modifiable maternal and fetal perinatal complications.

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**Keywords**
Angiotensin · Birth weight · Body adipose tissue · Body composition · Copeptin · Newborns · Nutrition · Pregnancy · Umbilical cord blood · Water homeostasis

## 1 Introduction

At the time of rapid development, such as an embryonic or fetal life, a number of organ structures and associated functions undergo programing, which determines the set point of physiological and metabolic responses to factors that carry into adulthood (Stout et al. 2015; Barker 1998). The environment "in utero" has been broadly studied in the framework of the Developmental Origins of Health and Disease (DOHaD) approach that evolved from epidemiological studies of infant mortality. According to the DOHaD hypothesis, increased susceptibility to diseases is partly shaped during fetal programing by early-life exposures through maternal diet, lifestyle, and other environmental conditions (Guéant et al. 2013). Nutritional status of the mother, which is an important factor that affects the programing of the body, involves factors such as maternal body composition, dietary and fluid intake, blood flow to the uterus and placenta, and fetal genes (Kwon and Kim 2017).

One of the major components of DOHaD is birth weight. Size at birth is an indicator of exposure to prenatal perturbations, which affect physical development and metabolic function. On one hand, evidence from epidemiological studies indicates that small size at birth is a risk factor for a range of metabolic problems, including high adult body mass index (BMI), insulin resistance, increased visceral adiposity, and impaired glucose tolerance (Stout et al. 2015; Calkins and Devaskar 2011). On the other hand, fetal macrosomia increases the risk of perinatal morbidity, mortality, and adverse developmental outcomes, especially obesity-related metabolic disorders later in life (Briana et al. 2017). Moreover, maternal obesity has been associated with increased risk of fetal macrosomia, neonatal adiposity, and metabolic syndrome in progeny (O'Connor et al. 2014). Thus, maternal body mass and body composition are modifiable risk factors of fetal macrosomia.

Several human studies have shown that the total body water accretion during pregnancy is associated with birth weight and it is considered a predictor of fetal well-being (Most et al. 2018; Larciprete et al. 2003). However, a direct relationship between total fluid intake, water intake, or intake of any other fluid type and pregnancy outcome and birth weight are rarely investigated. Experimental studies indicate that increased activity of the systems that play an essential role in the salt and water homeostasis, i.e., the sympathetic and renin-angiotensin-aldosterone pathways, and also enhanced oxidative stress or endothelin level has a substantial influence on the developmental programing of blood pressure in later life. A shift in the redox status toward the pro-oxidative side is observed in low-birth-weight humans and in the experimental models of developmental insult. The importance of oxidative stress and endothelin as mediators of increased cardiovascular risk is also demonstrated in animal studies (Alexander et al. 2015). In view of a paucity of data on factors shaping birth weight, this study seeks to define the potential role of maternal nutrition and water homeostasis in birth weight programing. To this end, maternal body composition, diet, and the serum content of copeptin, aldosterone, and angiotensin II were longitudinally assessed in pregnant women.

## 2 Methods

### 2.1 Study Population and Protocol

Seventy pregnant women up to the 12th week of pregnancy were enrolled into this study, conducted at the First Department of Obstetrics and Gynecology and the Department of Social Medicine and Public Health of Warsaw Medical University in Warsaw, Poland, from October 2014 to March 2017. All the patients were Caucasians and represented a college/university education level. Exclusion criteria were:

pre-pregnancy diabetes and hypertension, and heart, kidneys, liver, or endocrine disorders. The study was of a longitudinal nature. Patients were assessed in the 1st, 2nd, and 3rd trimester of pregnancy, i.e., up to week 12 and between week 15–week 20 and week 27–week 32 of gestation, respectively. In detail, the assessments were made, on average, at 11.6 week, 18.3 week, and 30.2 week. Out of the 70 pregnant women recruited for the study, 41 were lost to follow-up. Therefore, the final sample consisted of 29 pregnant women and 29 newborns.

At each visit, patients' clinical and demographic data were collected by means of a questionnaire. Anthropometric measures were taken and the diet was assessed. Skin-fold thicknesses was measured in triplicate on the right body side with a caliper (Holtain Ltd., Crosswell, UK) and the percentage of body fat (%BF) was calculated with the Yuhasz Body Density Equation (Shephard 1991). The newborns' weight was assessed at birth. The assessment of the diet was based on 7-day records of food consumption, which was checked by trained investigators during face-to-face interviews. Food consumption data was converted into energy and nutrient intake using the current "Polish Food Composition Tables" and "Diet 5" analysis software of the National Food and Nutrition Institute in Warsaw, Poland. Maternal fasting blood samples were taken twice in the 1st and 3rd trimesters. Mixed arteriovenous blood was taken in the newborns from the umbilical cord into pyrogen-free tubes. The blood was immediately centrifuged and the supernatant was frozen to −80 °C until further use. The plasma protein content was measured using the enzyme-linked immunosorbent assay (ELISA) kits for human angiotensin II (Cat. No. EKE-002-12), human copeptin (both purchased from Phoenix Pharmaceuticals Inc.; Burlingame, CA), and human aldosterone (ref. DE5298; Demeditec Diagnostics GmbH, Kiel, Germany), according to manufacturer's instructions. Sensitivities of the tests were 0.09 ng/mL, 0.12 ng/mL, and < 5.7 pg/mL, respectively.

Other data concerning the newborns consisted of gender, birth weight, body length, head circumferences, and the Apgar score. Normal body weight was considered as the 2500–4000 g range, with microsomia and macrosomia below and above those limits, respectively. Each newborn's birth weight was determined at the percentile line, using the World Health Organization (WHO) standards based on the gestational age, gender, and weight. Ponderal index (PI), a measure of leanness (corpulence) of a newborn calculated as a relationship between mass and height, was calculated. Additionally, small for gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA) categories were defined according to international standards based on the Intergrowth-21 Project that complemented the WHO standards (Villar et al. 2014).

## 2.2 Data Elaboration

Qualitative data were expressed as means ±SD and categorical data as counts and percentages. The Shapiro-Wilk test was used to assess data distribution and the Breusch and Pagan test to assess the possible nonlinear forms of heteroscedasticity. One-way ANOVA for repeated measures was used to assess differences in the energy and fluid intake, sodium, maternal fat, and blood content of biochemical indices measured across the three trimesters of pregnancy. Linear regression models were created to assess changes in the newborn's birth weight at the percentile line depending on the contents of copeptin and angiotensin in cord blood, and on the mother's adipose tissue content during the 1st trimester and the mother's body mass gain between the 1st and the 3rd trimester of pregnancy. The Wald test, with a significance set at $\alpha = 0.01$, was used to assess the significance of the explanatory variables in these models. Otherwise, a $p$-value <0.05 defined statistically significant differences. The analyses were performed using the R Statistical free software, IBM SPSS statistics v20 (IBM; Armonk, NY), Epi Info v7.2 – a free statistical package created by the Centers for Disease Control and Prevention (CDC, Atlanta, GA), and Microsoft Excel (Redmond, WA).

## 3 Results

The mean age of pregnant patients was 31.9 ± 3.9 years and the 1st trimester's BMI was 22.9 ± 2.6 kg/m$^2$. There were two cases of gestational diabetes diagnosed. Concerning the newborns, there were three macrocosmic ones, one microsomic, and another four were born preterm. Detailed clinical features of mothers and newborns are presented in Table 1.

### 3.1 Energy, Fluid, and Sodium Intakes and Maternal Adipose Tissue and Body Mass Changes Across Pregnancy

There were no appreciable differences noticed in the maternal energy, fluid and sodium intakes, and the percentage of adipose tissue across pregnancy trimesters (Table 2). In each trimester, a majority of patients reported sodium ingestion that was above the tolerable upper intake level (UL). About one half of patients gained more than 2.5 kg between the 1st and the 2nd trimester, with two pregnant women gaining > 7 kg. The analysis of a relationship between maternal micronutrients, macronutrients, and fluid intakes showed no association with birth weight of the progeny and with the maternal serum content of aldosterone, copeptin, and angiotensin II across the trimesters, nor with the cord blood content of these variables.

### 3.2 Content of Aldosterone, Angiotensin II, and Copeptin Content

The content of maternal aldosterone significantly increased in the 3rd trimester compared to the 1st trimester ($p < 0.01$). Interestingly, aldosterone in cord blood was approximately ten times higher than that in the maternal blood in the 3rd trimester. However, large discrepancies in the level of aldosterone were observed among the newborns. There were no significant differences between the maternal content of angiotensin II and copeptin across the trimesters. The cord blood aldosterone, angiotensin II, and copeptin did not differ between the newborns delivered vaginally or by C-section (Table 3).

### 3.3 Birth Weight and Umbilical Cord Blood Copeptin and Angiotensin II Content

To assess the relationship between different variables and either birth weight or birth weight percentile, several linear regression models were created. Two of them were statistically significant at an alpha level of 0.05, evaluated by the Wald test. There were no problems with multicollinearity of explanatory variables; the variance inflation factor (VIF) was <3. The error term was normal and homoscedastic and associations were statistically significant at a significance level < 0.05.

The first model explains the variability of birth weight with changes in the percentage of maternal body adipose tissue during the 1st trimester of pregnancy and with the umbilical cord blood angiotensin II content (Table 4). The birth weight was higher by 49.2 g per each 1% increase in body adipose tissue in women during the 1st trimester of pregnancy, with the other variables being constant in the model. Concomitantly, birth weight was lower by 177.7 g per each 0.1 ng/mL increase of cord blood angiotensin II content.

The second model explains the variability of birth weight percentile with changes in the percentage of maternal body adipose tissue during the 1st trimester of pregnancy, maternal body mass gain between the 1st and the 3rd trimester of pregnancy, and in the content of copeptin in cord blood (Table 4). The birth weight was higher by 2.6 percentile points per each 1% increase in body adipose tissue in women during the 1st trimester of pregnancy, with other variables constant in this model. Further, birth weight was higher by 3.3 percentile points per each 1 kg gain in mothers' body mass between the 1st and the 3rd trimester of pregnancy. Concomitantly,

**Table 1** Clinical characteristics of mothers ($n = 29$) and newborns ($n = 29$)

| Variables | Means ± SD or *n* (%) |
|---|---|
| Maternal age (years) | 31.9 ± 3.9 |
| Smoking before pregnancy | |
| Yes | 7 (24.1) |
| No | 22 (75.9) |
| Parity | |
| First | 15 (51.7) |
| Other | 14 (48.3) |
| Ethnicity | |
| Caucasian | 29 (100) |
| Education | |
| Higher education | 29 (100) |
| 1st trimester BMI[a] | 22.9 ± 2.6 |
| Mode of delivery | |
| Vaginal | 21 (72.5) |
| Cesarean section | 8 (27.5) |
| Gender of newborns | |
| Male | 19 (65.5) |
| Female | 12 (41.5) |
| Gestational age at birth (weeks) | 39.0 ± 1.5 |
| Birth weight (g) | 3511 ± 489.6 |
| Percentiles for birth weight by gestational age | 67.8 ± 28.9 |
| SGA | 1 (3.4) |
| AGA | 20 (69.0) |
| LGA | 8 (27.6) |
| PI | 2.07 ± 1.05 |

Categories of gestational age: *SGA* small gestational age, *AGA* appropriate gestational age, *LGA* large gestational age, *PI* Ponderal index

[a]Data concerning prepregnancy body mass unavailable

birth weight was higher by 13.6 percentile points per each 1 ng/mL increase of cord blood copeptin.

## 4 Discussion

Meeting the basic nutritional requirements, maintaining optimal gestational weight gain and maternal body composition by pregnant women are essential for health and well-being of both mother and child. This study aimed to investigate the maternal dietary energy and fluid intake and the serum content of aldosterone, angiotensin II, and copeptin across pregnancy trimesters in relation to birth weight of the progeny. Such an investigation seems rational to specify factors that could have a substantially influence on birth weight and, in turn, for the prevention of maternal and fetal complications.

The findings of the study failed to substantiate the presence of any appreciable associations between maternal diet or fluid intake, on the one side, and newborn's birth weight and the maternal or umbilical cord blood content of aldosterone, angiotensin II, and copeptin, on the other side, across the pregnancy trimesters. This result runs against a common recommendation for pregnant women to increase energy intake as the pregnancy progresses, especially in the 2nd and 3rd trimesters. In line with the present results, however, some previous studies have also failed to show the fulfilment of the recommendation, as longitudinal changes in pregnant women's caloric intake are unnoticeable (Abeysekera et al. 2016). Savard et al. (2018) have reported that dietary intakes are below the Canadian recommendations in 36.7% of the 79 pregnant women in the 1st, 63.3% in the 2nd, and 70.9% in the 3rd trimester

**Table 2** Trimester-specific maternal energy, fluid, sodium intakes, and the body adipose tissue (BAT) ($n = 26$)

| | 1st trimester | | | 2nd trimester | | | 3rd trimester | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | %Below EER, NV, AI, or UL | %Above EER, NV, AI, or UL | | %Below EER, NV, AI, or UL | %Above EER, NV, AI, or UL | | %Below EER, NV, AI, or UL | %Above EER, NV, AI, or UL | *p* |
| Energy intake (kcal/day) | | | | | | | | | | |
| EER | 1800–2050 | – | – | 2160–2410 | – | – | 2275–2525 | – | – | |
| Mean ± SD | 1855 ± 341 | 34.6 | 30.8 | 1805 ± 326 | 84.7 | 0 | 1856 ± 351 | 96.2 | 3.8 | 0.82 |
| Median | 1883 | – | – | 1885 | – | – | 1878 | – | – | |
| Maternal BAT (%) | | | | | | | | | | |
| **NV** | 17–28 | – | – | 17–28 | – | | 17–28 | – | – | |
| Mean ± SD | 24.2 ± 6.6 | 11.5 | 15.4 | 24.9 ± 5.9 | 7.7 | 38.5 | 27.1 ± 6.2 | 0 | 46.2 | 0.18 |
| Median | 22.1 | – | – | 24.5 | – | – | 25.9 | – | – | |
| Fluid intake (ml/day) | | | | | | | | | | |
| **AI** | 2300 | – | – | 2300 | – | – | 2300 | – | – | |
| Mean ± SD | 2168 ± 577 | 61.6 | 38.4 | 2447 ± 755 | 50.0 | 50.0 | 2621 ± 743 | 26.9 | 74.1 | 0.07 |
| Median | 2066 | – | – | 2296 | – | – | 2605 | – | – | |
| Sodium intake (mg/day) | | | | | | | | | | |
| **UL** | 2300 | – | – | 2300 | – | – | 2300 | – | – | |
| Mean ± SD | 3076 ± 791 | 19.2 | 80.8 | 3055 ± 578 | 7.7 | 92.3 | 3179 ± 782 | 7.7 | 92.3 | 0.80 |
| Median | 2998 | – | – | 3022 | – | – | 3101 | – | – | |

*EER* estimated energy requirement, consistent with Polish Institute of Food and Nutrition recommendations, to which an additional 360 or 475 kcal were added in the 2nd and 3rd trimesters; *AI* adequate intake, *NV* normal value, *UL* tolerable upper intake level. "–" depicts the lack of an established dietary reference intake value for a variable. Statistical evaluation performed with one-way ANOVA test for repeated measures

**Table 3** Serum content of aldosterone, angiotensin II, and copeptin in maternal blood in the 1st and 3rd trimester of pregnancy and in cord blood

| | 1st trimester | 3rd trimester | *p* | Cord blood |
|---|---|---|---|---|
| Aldosterone (pg/mL) | | | | |
| Mean ± SD | 374.0 ± 233.6 | 592.1 ± 157.9 | <0.01 | 6216.2 ± 10,429.1 |
| Median | 332.4 | 578.8 | | 2882.7 |
| | ($n = 28$) | ($n = 28$) | | ($n = 24$) |
| Angiotensin II (ng/mL) | | | | |
| Mean ± SD | 0.36 ± 0.21 | 0.29 ± 0.17 | 0.18 | 0.22 ± 0.14 |
| Median | 0.40 | 0.25 | | 0.17 |
| | ($n = 28$) | ($n = 29$) | | ($n = 26$) |
| Copeptin (ng/mL) | | | | |
| Mean ± SD | 0.45 ± 0.26 | 0.56 ± 0.61 | 0.40 | 0.95 ± 0.81 |
| Median | 0.38 | 0.36 | | 0.67 |
| | ($n = 28$) | ($n = 29$) | | ($n = 26$) |

**Table 4** Relationship between birth weight expressed in grams (Model 1) or birth weight percentiles expressed in points (Model 2) and the analyzed variables

| Model | Variable | Estimate | *p* |
|---|---|---|---|
| 1 | Maternal % of body adipose tissue during 1st trimester | 49.2 | 0.017 |
| | Cord blood angiotensin II | −177.7 | 0.019 |
| 2 | Maternal % of body adipose tissue during 1st trimester | 2.6 | 0.011 |
| | Maternal body mass gain between 1st and 3rd trimester of pregnancy | 3.3 | 0.069 |
| | Cord blood copeptin | 13.6 | 0.029 |

of pregnancy. In this study, these figures amounted to 33.3%, 84.7%, and 96.3% of the 29 pregnant women investigated in the respective trimesters of pregnancy.

Maternal weight gain during pregnancy is considered a key determinant of perinatal outcome. The guidelines of the Institute of Medicine (US) to optimize maternal, fetal, and infant health outcomes differentiate the gestational weight gain recommendations according to the prepregnancy BMI value. These guidelines also advocate that women achieve healthy body weight before pregnancy (Institute of Medicine US and National Research Council US 2009). Hulmán et al. (2015), using both quantile and linear regression statistical approaches, have reported that the gestational weight gain correlates with infant birth weight. In light of this report, the authors promote a strategy to mitigate the gestational weight gain on the population basis. However, O'Higgins et al. (2018) in a study encompassing 552 pregnant women have pointed out that when birth weight is subtracted from total gestational weight gain, the gestational weight gain loses the correlation with birth weight. Hence, a positive correlation between the gestational weight gain and birth weight may be accounted for by an antenatal contribution of fetal weight to gestational weight gain. In this study, there were only two women who displayed an excessive weight gain between the 1st and the 3rd trimesters.

Body adipose tissue can accurately reflect the maternal body composition and is considered a better predictor of birth weight than BMI. There are reports showing that maternal body adipose tissue is a major determinant of birth weight (Wang et al. 2017; Toro-Ramos et al. 2016; O'Connor et al. 2014). In line with those reports, we found in this study that the percentage of maternal adipose tissue in early stages of pregnancy has a relation to birth weight. Notwithstanding the numerous studies and meta-analysis made on the subject, no consensus has ever been reached regarding the optimal gestational weight gain for different maternal BMI categories (Robillard et al. 2018). Yet, prevention of

overweight and obesity in women of child-bearing age seems a reasonable approach. Findings from the Helsinki Birth Cohort Study show that a higher maternal BMI associates with less favorable body composition in the offspring (Eriksson et al. 2015). It is accepted that both body weight and composition in women of child-bearing age are essential factors in the DOHaD hypothesis.

Hydration during pregnancy is another such factor. In women with normal amniotic fluid volume, oral hydration increases the amniotic fluid index by approximately 16%, whereas fluid restriction decreases this index by 8% (Mulyani et al. 2017). In this study, we did not confirm the presence of a relation between fluid intake and birth weight, serum angiotensin, aldosterone, and copeptin. However, the women of this study failed to follow the fluid intake recommended for each trimester of pregnancy. Fluid intake was below that recommended in 61.6% of women in the 1st, 50.0% the in 2nd, and 26.9% in the 3rd trimesters. Bardosono et al. (2016) have also reported that 42% out of the 300 pregnant Indonesian women fail to reach the adequate intake of water. In light of these observations, it seems important to promote adequate water intake during pregnancy, especially in its early stages. This issue needs to be further explored in studies focusing on amniotic fluid index and body water balance during pregnancy.

The renin-angiotensin-aldosterone system (RAAS) plays an essential role in the salt and water homeostasis. Angiotensin II is the most biologically active peptide in the system and exerts its effects on sodium reabsorption and vasoconstriction. Data on the effects on the in utero fetal development of angiotensin II are scarce during pregnancy (Svitok et al. 2017). In this study, there was no appreciable relation between salt and water intake across pregnancy trimesters, on the one side, and the maternal serum angiotensin II and aldosterone content, on the other side. We found, however, that increasing cord blood angiotensin II correlated with decreasing birth weight. This finding is somehow in line with an experimental study that has shown that the kidney tissue angiotensin II content is significantly higher in the intrauterine growth-restricted rats than that in healthy rats (Chou et al. 2008). Other studies have also reported the increased activity of plasma renin, angiotensin I, and angiotensin II in low-birth-weight lambs (Wang et al. 2015). The suggestion arises that small size at birth is associated with increased risk of adult cardiovascular disease in later life and this association may partly be a consequence of early disordered programing of the RAAS.

This study shows that maternal plasma aldosterone was significantly higher in the 3rd trimester compared to the 1st trimester of pregnancy, and it was much higher in the cord blood compared to maternal blood. These results are in line with those of some previous studies in which the increased aldosterone over the pregnancy course coincides with increasing sodium retention (Martinerie et al. 2009; Beitins et al. 1972). This explanation seems a viable plausibility in view of sodium intake much above the tolerable upper limit in the majority of our patients (Table 2), although we did not directly assess the magnitude of sodium retention. The increase in aldosterone may be related to the activation of the RAAS system in pregnancy, which is strongly expressed in case of sodium retention. There are other possible explanations of hyperaldosteronism during pregnancy, such as increased plasm content of progesterone and estradiol and thus increased excretion of these hormones, causing antagonism to aldosterone excretion at the level of renal tubular system (Katz and Kappas 1967).

This study also shows a markedly higher level of aldosterone in cord blood compared to maternal blood. That confirms older findings showing that fetal adrenals are capable of synthesizing and secreting aldosterone, as of week 15 gestation, independently of a small portion of it crossing the placenta (Bayard et al. 1970; Dufau and Villee 1969). Further, Martinerie et al. (2009) have shown that healthy newborn infants exhibit partial resistance to aldosterone with high plasma levels of aldosterone and renin. In contradistinction, Traversa et al. (2018) have reported that compared to the maternal blood, cord blood contains less aldosterone, cortisol, and androstenedione, accompanied by a greater content of

upstream precursors, which suggests that birth involves a limiting step in the adrenal steroid biosynthesis.

Arginine vasopressin is yet another key player in the water homeostasis (Bardosono et al. 2016). The measurement of vasopressin is rather difficult and it is subject to considerable preanalytical errors due to the hormone's short half-life and instability in the serum. Copeptin, a stable C-terminal fragment of pre-provasopressin, is considered a stable surrogate for vasopressin as a potential stress marker in newborns, reflecting also a degree of hydration, in the early adaptation period to life (Jarosz-Lesz and Maruniak–Chudek 2015; Morgenthaler et al. 2008). Plasma copeptin content increases in response to increased osmolality and dehydration and thus is of relevance in regulating fluid balance and vascular tone (Benzing et al. 2011). In this study, there was no relation between copeptin content and maternal water intake. However, given the significance of glucose and insulin in fetal growth and the fundamental role of copeptin in insulin metabolism, it is reasonable to assume that the hormone plays a regulatory role in excessive fetal growth (Lukaszyk and Malyszko 2015). This study indeed shows that copeptin in cord blood correlated with birth weight, which is in line with the known relation between vasopressin release and increased adipose tissue deposition (Briana et al. 2016).

Koch et al. (2011) have assessed the content of various vasoactive and natriuretic mediators, including copeptin, in the blood of healthy adults and in cord blood. In that study, the content of copeptin is significantly higher in cord blood. Further, those authors have reported that cord blood copeptin was substantially elevated in case of vaginal delivery versus elective C-section, exceeding even the values described in the population of critically ill adult patients. The present findings were partly in line with that study, showing that cord blood copeptin was about twice as high as that in the maternal blood. In contradistinction, we found that the content of cord blood copeptin did not depend on the way of baby delivery.

A limitation of this study is a small population size. Also, an observational design of the study precluded the establishment of causality. However, we believe the study was warranted in the face of a paucity of information on the factors underlying fetal weight and the contentiousness of existing literature results on the subject. In synopsis, fetal birth weight associates with the maternal body adipose tissue during the 1st trimester of pregnancy. Further, birth weight correlates positively with copeptin and adversely with angiotensin II in cord blood. The clinical relevance of these observations is not entirely clear and should be explored using alternative study designs. We conclude that the present findings may be helpful in the assessment of a critical level of body adipose tissue in women of child-bearing age, above which there would appear a potentially modifiable risk of macrosomia. The female population of child-bearing age should be kept updated with the continually progressing nutritional savvy to prevent maternal and fetal perinatal complications.

**Conflicts of Interest** The authors declare no conflicts of interest in relation to this article.

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved by an institutional Ethics Committee.

**Informed Consent** Written informed consent was obtained from all individual participants included in the study.

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