Journal of Perinatology (2018) 38:489–495
https://doi.org/10.1038/s41372-018-0053-7

ARTICLE

Adiponectin, insulin and leptin levels in the cord plasma of the neonates from adolescent and adult mothers and their relationship with anthropometric parameters and fetal sex-gender

Michele Gonçalves Santana[1] · Patricia Coelho de Velasco[1] · Olívia Rebelo Coelho de Oliveira[1] · Raquel Espírito Santo[1] · Flavia Spreafico[1] · Lívia Belcastro de Almeida[1] · Fatima Lucia de Carvalho Sardinha[1] · Maria das Graças Tavares-do-Carmo[1]

Received: 7 August 2017 / Accepted: 4 December 2017 / Published online: 7 February 2018
© Nature America, Inc., part of Springer Nature 2018

Abstract

Objective This cross-sectional study aimed to evaluate the association between leptin, insulin and adiponectin levels and anthropometric measurements of term newborns of adolescent and adult mothers.

Study Design Umbilical cord plasma samples were obtained from 80 healthy term neonates (40 from teenagers and 40 from adult mothers) and adiponectin, insulin and leptin concentrations were measured.

Results Cord plasma adiponectin levels were higher in the boys from adult mothers than in the boys of the adolescent ($p < 0.05$), while plasma leptin levels in the boys of the adults were significantly lower ($p < 0.05$) than those of girls from both groups. Univariate correlation analysis showed that leptin umbilical cord plasma levels were positively associated with birth weight in neonates from adolescents and adults. Multiple linear regression analysis revealed that leptin levels showed significant positive predictor for birth weight specifically in the adult mother.

Conclusion Gestational age, but not adipokines, showed to be a significant positive predictor factor of birth weight in adolescent pregnancy.

Introduction

Fetal growth is the result of integrated interplay among genetic, nutritional, and endocrine factors[1]. Insulin is one of the best known key regulators of fetal growth, but recently some adipokines have also emerged as a link among maternal metabolism, insulin resistance, and fetal development[2]. Studies in adult pregnant women have reported that adiponectin and leptin levels in umbilical cord blood directly correlate with fetal weight and adiposity at birth[3–6]. In fact, adipokines has received significant interest as a potential programming factor. In particular, changes in the leptin profile in early life are associated with altered susceptibility to obesity and metabolic disorders in adulthood[7,8]. Mantzoros et al.[9] have recently shown that lower levels of cord blood leptin predict higher body mass index (BMI) at the age of 3 years, while higher cord blood adiponectin was associated with higher central adiposity. Moreover, sex differences may be particularly important, and some studies revealed that female neonates had significantly higher levels of umbilical cord plasma leptin than males[10–12]. However, there is a remarkable lack of similar studies regarding pregnant adolescents.

Adolescent pregnancy is associated with significant medical, nutritional, social, and economic risk for mothers and their infants throughout the world[13,14]. It is associated with an increased risk of adverse outcomes such as maternal and neonatal mortality, cesarean section, preterm birth and low birth weight[15–17]. These poor outcomes may be explained by a possible physical and psychological immaturity for reproduction in adolescents[13]. In addition, epidemiological associations have been found to exist between lower birth size and a greater risk of death in later life from

Electronic supplementary material The online version of this article (https://doi.org/10.1038/s41372-018-0053-7) contains supplementary material, which is available to authorized users.

✉ Maria das Graças Tavares-do-Carmo
tcarmo@editema.com.br

[1] Laboratório de Bioquímica Nutricional, Instituto de Nutrição Josué de Castro da Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil

cardiovascular disease and type 2 diabetes mellitus[17–19]. Moreover, crucial sex differences exist in long-term trends in obesity among different ethnic groups[20].

Therefore, the purpose of this study was to investigate the relationship between venous umbilical cord plasma adiponectin, leptin and insulin levels and anthropometric markers at birth in a group of Brazilian term healthy newborns of adolescent and adult mothers. Furthermore, we also analyzed the sex differences among the studied parameters.

Subjects and methods

Ethics statement

Consent forms were signed by the mothers or their legal guardians (in the case of the adolescents) and the study protocol was approved by the ethics committees of Fernandes Figueira Institute/Oswaldo Cruz Foundation and the Maternity School of the Federal University of Rio de Janeiro (No. 12/2008, CAAE: 0008.0.361.000-08).

Participants

Forty newborns of adolescent mothers between the ages of 15 and 19 years and forty from adults mothers between the ages of 20 and 40 years, participated in the study. Neonates were randomly recruited at birth from the maternity ward of the Fernandes Figueira Institute/Oswaldo Cruz Foundation and the Maternity School of the Federal University of Rio de Janeiro from January 2014 to March 2016. All of the pregnant women who participated were healthy, non-smokers, free of chronic diseases (such as diabetes mellitus and systemic arterial hypertension), did not use drugs or alcohol, had a term and single gestations and had no fetal complications (such as abnormal formation and anencephaly). Newborns with risk factors (maternal diabetes, stressful delivery, infection, etc.), were excluded from the study.

Anthropometric measurements

A questionnaire was applied to obtain socio-demographic, anthropometric measurements of mothers, obstetric data and information regarding lifestyle. Gestational age (GA) at delivery was calculated according to the last menstrual period and confirmed by ultrasound examination during the first trimester or early second trimester. The variables of the neonates included birth weight (BW), birth length (BL), head circumference, gestational age (GA), and BW/BL ratio. We also used combinations of two anthropometric factors: Ponderal Index (PI), and Body Mass Index (BMI). PI and BMI are expressed by the following formulas: PI=body weight (g)/[body length (cm)]$^3 \times 100$ and BMI=body weight (kg)/birth length^2 (m). All birth outcome variables were measured according to standard hospital procedures and the local nursing staff carried out anthropometric measurements of infants at delivery. The body weight of each neonate and placental weight were determined to the nearest 1 g using an electronic scale. Body length was determined to the nearest 0.1 cm in the supine position with a length board. Head circumference was determined with a plastic tape to the nearest 0.1 cm.

Sample collection and biochemical analysis

The venous cord blood samples were obtained prior to the expulsion of the placenta, with EDTA as anticoagulant, through manual expression of the blood. All plasmas were obtained by centrifugation at $4000 \times g$ for 10 min in a microcentrifuge at room temperature and stored in multiple aliquots at −80 °C until biochemical assays. Cord plasma insulin, leptin and total adiponectin concentrations were measured by a commercially available ELISA assay kits (LINCO Research, St Louis, USA). The sensitivity limits of the studies were 0.78 µg/mL for adiponectin, 2.0 µU/mL for insulin and 0.5 ng/mL for leptin. The intra- and inter-assay coefficients of variation (CV) ranged from 5 to 7%.

Statistical analysis

All statistical analyses were performed using software (SPSS 13.0; IBM Corp, Armonk, NY). We performed the Kolmogorov–Smirnov test to verify the normality of distribution of the quantitative variables. Normally distributed data were expressed as means ± SD and $p < 0.05$ was considered to be statistically significant. Variables with a skewed distribution were represented as median (interquartile range). Categorical variables were reported as numbers (percentages). We compared characteristics between the neonates of adolescent and adult mothers using a non-parametric *t*-test or the Mann–Whitney test. Associations between cord plasma levels of adiponectin, insulin and leptin were evaluated using Pearson or Spearman correlation analyses and will be presented as supplementary data in this study. Multiple regression analysis was used to analyze the influence of multiple factors (sex, gestational age, pre-gestational maternal weight, maternal stature, total maternal weight gain during gestation, placenta weight, cord levels of insulin, adiponectin and leptin) on weight, length, head circumference and PI and BMI.

Table 1 Clinical and anthropometric characteristics of the neonates at birth

	Adolescent	Adult		Adolescent		Adult	
	All births ($n = 40$)	All births ($n = 40$)	p-value	Males ($n = 23$)	Females ($n = 17$)	Males ($n = 21$)	Females ($n = 19$)
Gestacional age (wk)	39.0 ± 1.2	39.9 ± 1.1	0.002	39.5 ± 1.3	38.9 ± 1.1 #	39.7 ± 1.1	40.1 ± 1.1
Placental weight (g)	630 ± 112	611 ± 123	0.14	641 ± 123	615 ± 94	621 ± 115	600 ± 133
Birth weight (BW) (g)	3214 ± 391	3302 ± 432	0.34	3300 ± 441	3096 ± 285*	3463 ± 454	3124 ± 333*
Birth length (BL) (cm)	50.1 ± 2.6	48.4 ± 2.3	0.003	50.9 ± 2.5#	49.0 ± 2.2	49.3 ± 1.8	47.4 ± 2.4
BW/BL (g/cm)	64.2 ± 1.1	68.6 ± 7.0	0.0065	64.8 ± 7.7	63.3 ± 5.7 #	70.6 ± 8.1	66.3 ± 4.6
PI[a]	2.6 ± 0.4	2.9 ± 0.3	<0.0001	2.5 ± 0.4*	2.7 ± 0.4#	2.91 ± 0.3	3.0 ± 0.2
BMI (Kg/m^2)[b]	12.9 ± 1.5	14.2 ± 1.3	<0.0001	12.8 ± 1.6*	12.9 ± 1.4*#	14.3 ± 1.6	14.0 ± 0.9
Birth head circumference (cm)	34.0 ± 2.4	34.5 ± 1.4	0.14	34.3 ± 2.9	33.6 ± 1.5*	34.9 ± 1.3	33.0 ± 1.3*

Values are mean ± SD. *different from boys adults, #different from girls adults

[a]PI=body weight(g)/[body length(cm)]^3 × 100

[b]BMI=body weight(kg)/birth length^2(m)

Results

Clinical characteristics and anthropometric measurements of newborns

In the group of infants born of adolescent mothers, the gestational age was lower compared to infants born of adult mothers ($p < 0.05$) (Table 1), but when stratified to sex, only the female neonates of adolescents showed lower gestational age (mean ± SD: 38.9 ± 1.1 wk n = 17) than female neonates of adult mothers (40.1 ± 1.1 wk; $p < 0.05$ $n = 19$, respectively). There was no significant difference in mean birth weight and head circumference between infants of adolescent and adult mothers. However, mean birth weight and birth head circumference of the female newborns from both groups were significantly lower than in male infants of adult mothers ($p < 0.05$). Mean BL was significantly higher in the infants of adolescents than in those of adult mothers ($p < 0.05$). However, BW/BL ratio and the values of the ponderal index (PI) and BMI were significantly lower in newborns of adolescents when compared with adult mothers, and these differences were observed in both, male and female infants of adolescent mothers.

Biochemical characteristics

Mean cord plasma levels of adiponectin were significantly lower ($p < 0.05$) in the newborns of adolescent (39.3 ± 21.2 μg/mL) than adult mothers (47.5 ± 21.2 μg/mL), while leptin and insulin levels were not statistically different between groups (Table 2). When stratified by sex, mean cord plasma adiponectin concentration was lower ($p < 0.05$) in the male newborns of adolescent mothers (34.0 ± 17.0 μg/mL) than in males of adult mothers (52.4 ± 23.3 μg/mL). Mean cord blood leptin concentration was significantly lower ($p < 0.05$) in male newborns from adult mothers (9.9 ± 7.2 ng/mL) than in female newborns of the adolescent (12.1 ± 6.3 ng/mL) and the adults mothers (17.5 ± 12.8 ng/mL).

Univariate analyses

In pregnant teenagers, BW correlated with pre-pregnancy BMI ($r = 0.32$, $p < 0.05$), the total weight gain during pregnancy ($r = 0.39$, $p < 0.05$) and the gestational age at birth ($r = 0.54$, $p < 0.05$). We also found a positive association between placental weight and birth weight and head circumference ($r = 0.48$ and $r = 0.33$, $p < 0.05$, respectively). Similarly, the head circumference was positively associated with gestational age at birth ($r = 0.33$, $p < 0.05$). In neonates of adults mothers placental weight was associated with weight at birth ($r = 0.56$, $p < 0.05$) (data not shown).

The male newborns from adolescent mothers showed a significant positive association between leptin levels and birth weight ($r = 0.58$; $p = 0.004$), and head circumference ($r = 0.60$; $p = 0.003$). Placental weight was associated with weight at birth ($r = 0.52$; $p = 0.011$) and head circumference ($r = 0.49$; $p = 0.019$). In addition, gestational age at birth was significantly associated with birth weight ($r = 0.53$, $p = 0.009$). In female newborns of adolescent mothers, leptin levels positively correlated with adiponectin levels ($r = 0.66$, $p < 0.05$) (Supplementary Material I).

In female neonates from adult mothers, adiponectin concentrations in cord blood were inversely correlated with maternal pre-gestational BMI. We observed significant correlations between cord blood leptin concentration and

Table 2 Concentrations of adiponectin, insulin and leptin in cord blood

	Adolescent	Adult		Adolescent		Adult		
	All births ($n = 40$)	All births ($n = 40$)	p-value	Males ($n = 22$)	Females ($n = 17$)	Males ($n = 21$)	Females ($n = 19$)	p-value
Adiponectin (μg/mL)	39.3 ± 21.2 (36.3)	47.5 ± 21.2 (47.5)	**0.04**	34.0 ± 17.0 (28.7)	46.2 ± 24.4 (43.8)	52.4 ± 23.3 * (55)	42.1 ± 17.6 (40)	**0.005**
Leptin (ng/mL)	11.5 ± 8.5 (9.2)	13.5 ± 10.1 (8.5)	0.89	11.0 ± 10 (8.9)	12.1 ± 6.3 (11.5)	9.9 ± 7.2 (6.6)#Δ	17.5 ± 12.8 (14.1)	**0.001**
Insulin (μU/mL)	6.6 ± 5.2(4.9)	5.4 ± 4.1 (4.1)	0.45	6.0 ± 5.2 (4.8)	7.3 ± 8.6 (5.0)	6,3 ± 5,4 (4.1)	4.3 ± 1.4 (4.1)	0.50

Values are mean ± SD (median). *different from boys (adolescent),[#] different from girls (adolescent), Δ different from girls (adults).

Table 3 Significant coefficients of multiple regression of predictors of antropometric measurements at birth in the group of newborns from adults ($n = 40$)

Predictors factors	Weight (g)		Length (cm)		Head circumference (cm)		PI (g/cm^3)		BMI (kg/m^2)	
	0.146[a] ($p < 0.001$)		0.611[a] ($p < 0.001$)		0.458[a] ($p < 0.001$)		0.168[a] ($p < 0.046$)		0.291[a] ($p < 0.004$)	
	Beta	p	Beta	p	Beta	p	Beta	p	Beta	p
Sex (boys)	405.29	**0.002**†	3.48	**0.000**†	1.38	**0.012**†	0.164	NS	−0.077	NS
Placental weight (g)	2.13	**0.000**†	0.00	NS	0.00	NS	0.001	**0.011**†	0.007	**0.000**†
Cord adiponectin (μg/mL)	−1.46	NS	−0.04	**0.023**†	0.00	NS	0.004	NS	0.010	NS
Cord leptin (ng/mL)	10.46	**0.038**†	0.11	**0.001**†	0.03	NS	−0.006	NS	−0.002	NS

NS not significant, *PI* Ponderal index, *BMI* Body mass index

†p <0.05

[a]Adjusted R^2

birth weight ($r = 0.62$, $p = 0.005$) and birth length ($r = 0.74$, $p = 0.000$) and head circumference ($r = 0.65$; $p = 0.003$). In male newborns, we detected significant correlations between cord blood leptin concentration and birth weight ($r = 0.63$, $p = 0.002$) and birth length ($r = 0.55$, $p = 0.012$). We also observed a significant positive correlation between placental weight and birth weight ($r = 0.77$, $p = 0.000$) and gestational age at birth was significantly associated with birth length in male of adult mothers ($r = 0.47$, $p = 0.036$) (Supplementary Material II).

Multivariate linear regression analysis

Multiple linear regression analysis revealed that only leptin levels showed significant positive predictor for birth weight and birth length, specifically in newborns of adult mothers (Table 3). Moreover, the sex of the neonates was shown to be a significant positive predictor for all anthropometric measurements at birth. Also, the weight of the placenta proved to be a significant positive predictor of birth weight. For the adolescent group (data not shown), the gestational age showed to be a significant positive predictor factor of birth weight ($\beta = 163.35$; $p < 0.05$).

Discussion

To our knowledge, there are few studies about the influence of cord blood leptin, adiponectin, and insulin levels for growth in neonates of adolescent mothers, especially comparing with neonates of adult mothers and the correlation according to sex. Here we show that cord blood adiponectin levels in neonates of adolescent mothers were significantly lower compared with adult levels. Chan and colleagues[21] in analyzing the concentrations of adiponectin in the umbilical cord of adult mothers found mean values of 46.9 µg/mL, similar values to that which we found for adiponectin in the umbilical cord of newborns of adults (47.5 µg/mL) and relatively greater (20%) than the levels observed for the neonates of the adolescents (39.3 µg/mL). On the other hand, the insulin levels were similar between groups of infants at birth, suggesting that insulin alone does not explain changes in adiponectin levels. The lower levels of adiponectin in cord blood of adolescents is probably due to a lack of negative feedback on adiponectin production resulting from an absence of adipocyte hypertrophy, a low percentage of body fat or a different distribution of fat depots in newborns of adolescent mothers[22].

In our present study, the levels of adiponectin were significantly lower in male neonates of adolescents mothers compared with males neonates of adult mothers. In addition, the boys of adolescent mothers were those who had the lowest BMI and PI. It is possible that the reduced adipose mass and the prevalence of small adipocytes in the adipose tissue of newborns of adolescent mothers may explain the lower levels of adiponectin present in these neonates. Soriguer Escofet and colleagues[23] verified two populations of adipose cells in newborns—small adipocytes which contain no fat, and larger adipocytes which contain fat but which were smaller in diameter than the fat cells of adults. Furthermore, the percentage of body fat has been found to be significantly lower in neonates (13%) as compared to children or adults (25–30%)[24]. These findings suggest that the reduced levels of adiponectin in cord blood of adolescents may derive from this decreased adipose tissue and that, at birth, adiponectin is largely derived from fetal adipose tissue. Adiponectin levels are referred to be lower in preterm infants at discharge compared to full term, probably due to decreased adiposity[25]. In addition, in the group of infants born of adolescent mothers, the gestational age was lower compared to infants born of adult mothers, suggesting that gestational age is important for development of adipose tissue and, therefore influences neonatal adiponectin levels. On the other hand, in the regression model, adiponectin levels in cord blood was found to be negative predictor factor ($p < 0.05$) for length at birth in the adult group. In fact, the neonates of the adults were significantly smaller in length than the neonates of the adolescents. A negative association between cord adiponectin levels and pre-pregnancy maternal BMI was also found in the adult group. Thus, these data suggest that adiponectin levels in the cord blood may be a key adipokine for control of fetal adiposity.

Leptin levels have been widely accepted as a marker for neonatal fat mass, and its receptors are expressed in several fetal tissues[26,27] suggesting that leptin may exert biological functions in the fetus and/or early in life. In this study, cord leptin concentration was associated with birth weight of the newborn ($r = 0.38$, $p < 0.05$) and placental weight ($r = 0.37$, $p < 0.05$) in adolescents and with birth length ($r = 0.36$, $p < 0.05$) from adult mothers. Moreover, the results in the intergroup comparisons, the leptin from the boys of the adults was also significantly less than that observed in the girls of the adolescents and the adults. Similar result was described by Inoue and colleagues[28], revealing a difference between boys and girls in regard to the concentrations of leptin in the umbilical cord, but not for adiponectin. In this study, boys from adolescent mothers were potentially more vulnerable to cord adiponectin concentration and not, cord leptin levels, than boys from adult mothers. The evidence of a positive association between cord leptin levels and the birth weight of male but not of female newborn infants from adolescents was also reported here. Although further studies are necessary to investigate a possible causal relationship between cord adiponectin and leptin, our finding raises the possibility that cord leptin may play an important role in metabolic homeostasis during fetal life.

The differences in cord leptin concentrations between male and female neonates may be explained by differences in fat mass[23], a sex-based difference in the regional adipose tissue regulation of leptin production[11] and sex hormone levels, such as testosterone[29]. Other authors also suggested that boys being heavier than girls, their body weight likely reflect heavier muscle bulk and skeleton, whereas higher leptin concentrations in girls are correlated with more subcutaneous fat[30]. However, Pardo and colleagues[31] observed that the difference in the concentration of leptin in newborns, according to sex, is present even when comparing neonates of the masculine and feminine sex who have the same characteristics in terms of weight, length, and weight index. Therefore, we can speculate that differences in cord leptin concentration is likely to be due to both relative body composition and fat distribution, which are different in male and female infants, regardless of whether pregnant adolescent or adult.

Pregnant teenager and her fetus are in critical stages of growth during the gestational period. Here we show that pre-pregnancy BMI was significantly associated with birth weight in adolescent mothers. Moreover, total gestational weight gain was significantly associated with weight and length at birth only in the group of adolescents. After stratification by sex, boys and girls born of adolescents showed positive correlation between anthropometric variables of the mother and neonatal anthropometric outcomes, suggesting association between quality of prenatal care and good outcome for the newborns as previously proposed in others studies with pregnant adolescent[14,32].

After multiple regression analysis our findings revealed differences between groups. For the adolescents, only gestational age at birth was found to be a positive predictor factor and significant to the anthropometric measurements of the neonates, specifically in regard to weight at birth. For the neonates of adults mothers, sex proved to be a positive predictor factor and significant to all of the neonatal anthropometric parameters, while the weight of the placenta was a positive predictor and significant only for weight at birth. In addition, leptin was shown to be a variable predictor for weight ($\beta = 10.46$; $p < 0.05$) and length at birth ($\beta = 0.11$; $p < 0.05$). A study of adult Japanese women showed that higher levels of cord leptin appeared to correlate with an increased amount of fats accumulated in the fetus, resulting in higher BMI and PI[33].

Finally, some limitations of the study deserve comments. The size of this cohort may limit the identification of the correlation between cord adipokines levels and anthropometry. In addition, investigations of adiponectin multimers may be required to clarify such associations, because adiponectin mainly exists in a high-molecular-weight form (HMW-ad), which may be the active form.

In summary, to our knowledge, this is the first study to compare the concentrations of adipokines in cord umbilical plasma of neonates born of adolescent and adult mothers and the findings suggest that pregnant adolescents from a Public Maternity Hospital in the city of Rio de Janeiro, Brazil are at increased risk for shortened gestation. It can reflect alterations of anthropometric parameters in the newborn and, therefore influences adipokine secretion and other consecutive metabolic and endocrine factors. The adipokines studied revealed particularities when we analyzed the newborns of adolescent and adult mothers, as well as in their stratification according to sex. It is suggested that future longitudinal studies should be performed to compare the concentrations of these adipokines in neonates born of adolescent and adult mothers in order to confirm the existence of a sex-specific relationship between cord blood adiponectin levels in neonates of adolescent mothers and fetal fat development.

Acknowledgements This study was supported by the Brazilian Research Council (Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq) and Fundação de Amparo a Pesquisa do Rio de Janeiro (FAPERJ).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Burton GJ, Fowden AL, Thornburg KL. Placental origins of chronic disease. Physiol Rev. 2016;96:1509–65.
2. Briana DD, Malamitsi-Puchner A. The role of adipocytokines in fetal growth. Ann N Y Acad Sci. 2010;1205:82–7.
3. Petridou E, Mantzoros CS, Belechri M, Skalkidou A, Dessypris N, Papathoma E, et al. Neonatal leptin levels are strongly associated with female gender, birth length, IGF-I levels and formula feeding. Clin Endocrinol. 2005;62:366e71.
4. Mantzoros C, Petridou E, Alexe DM, Skalkidou A, Dessypris N, Papathoma E, et al. Serum adiponectin concentrations in relation to maternal and perinatal characteristics in newborns. Eur J Endocrinol. 2004;151:741e6.
5. Sivan E, Mazaki-Tovi S, Pariente C, Efraty Y, Schiff E, Hemi R, et al. Adiponectin in human cord blood: relation to fetal birth weight and gender. J Clin Endocrinol Metab. 2003;88:5656e60.
6. Tsai PJ, Yu CH, Hsu SP, Lee YH, Chiou CH, Hsu YW, et al. Cord plasma concentrations of adiponectin and leptin in healthy term neonates: positive correlation with birth weight and neonatal adiposity. Clin Endocrinol. 2004;61:88e93.
7. Vickers MH1, Sloboda DM. Leptin as mediator of the effects of developmental programming. Best Pract Res Clin Endocrinol Metab. 2012;26:677–87.
8. Kajantie E, Hytinantti T, Hovi P, Andersson S. Cord plasma adiponectin: a 20-fold rise between 24 weeks gestation and term. J Clin Endocrinol Metab. 2004;89:4031–6.
9. Mantzoros CS, Rifas-Shiman SL, Williams CJ, Fargnoli JL, Kelesidis T, Gillman MW. Cord blood leptin and adiponectin as predictors of adiposity in children at 3 years of age: a prospective cohort study. Pediatrics. 2009;123:682e9.

10. Matsuda J, Yokota I, Iida M, Murakami T, Naito E, Ito M, et al. Serum leptin concentration in cord blood: relationship to birth weight and gender. J Clin Endocrinol Metab. 1997;82:1642–4.
11. Tome MA, Lage M, Camina JP, Garcia-Mayor RV, Dieguez C, Casanueva FF. Sex-based differences in serum leptin concentrations from umbilical cord blood at delivery. Eur J Endocrinol. 1997;137:655–8.
12. Tung WK, Lin SJ, Hwang YS, Wu CM, Wang YH, Tsai WH. Association of cord plasma leptin with birth size in term newborns. Pediatr Neonatol. 2009;50:255–260.
13. Elfenbein DS, Felice ME. Adolescent pregnancy. Pediatr Clin North Am. 2003;50:781–800.
14. Conde-Agudelo A, Belizán JM, Lammers C. Maternal-perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: cross-sectional study. Am J Obst Gynecol. 2005;192:342–9.
15. Malamitsi-Puchner A, Boutsikou T. Adolescent pregnancy and perinatal outcome. Pediatr Endocrinol Rev. 2006;3(Suppl 1):170–1.
16. Alves JBG, Cisneiros RMR, Dutra LPF, Pinto RA. Perinatal characteristics among early (10–14 years old) and late (15–19 years old) pregnant adolescents. BMC Res Notes. 2012;5:531.
17. Forsen T, Eriksson J, Tuomilehto J, Reunanen A, Osmond C, Barker D. The fetal and childhood growth of persons who develop type 2 diabetes. Ann Intern Med. 2000;133:176–82.
18. Eriksson JG, Forsen T, Tuomilehto J, Jaddoe VWV, Osmond C, Barker DJP. Effects of size at birth and childhood growth on the insulin resistance syndrome in elderly individuals. Diabetologia. 2002;45:342–8.
19. Gillman MW. Developmental origins of health and disease. N Engl J Med. 2005;353:1848e50.
20. Wisniewski AB, Chernausek SD. Gender in childhood obesity: family environment, hormones, and genes. Gend Med. 2009;6 (Suppl 1):76–85.
21. Chan TF1, Yuan SS, Chen HS, Guu CF, Wu LC, Yeh YT, et al. Correlations between umbilical and maternal serum adiponectin levels and neonatal birth weights. Acta Obstet Gynecol Scand. 2004;83:165–9.
22. Savino F, Petrucci E, Nanni G. Adiponectin: an intriguing hormone for paediatricians. Acta Paediatr. 2008;97:701–5.
23. Soriguer Escofet FJ, Esteva de Antonio I, Tinahones FJ, Pareja A. Adipose tissue fatty acids and size and number of fat cells from birth to 9 years of age – a cross-sectional study in 96 boys. Metabolism. 1996;45:1395–401.
24. Schmelzle HR, Fusch C. Body fat in neonates and young infants: validation of skinfold thickness versus dual-energy X-ray absorptiometry. Am J Clin Nutr. 2002;76:1096–1100.
25. Palchevska S, Krstevska M, Shukarova E, Aluloska N, Jakimoska M, Kocevski D, et al. Comparing preterm and term newborns serum adiponectin and leptin concentrations and their correlations with anthropometric parameters. Maced J Med Sci. 2012;5:317–23.
26. Clapp JF, Kiess W. Cord blood leptin reflects fetal fat mass. J Soc Gynecol Investig. 1998;5:300–3.
27. Lepercq J, Challier JC, Guerre-Millo M, Cauzac M, Vidal H, Hauguel-de Mouzon S. Prenatal leptin production evidence that fetal adipose tissue produces leptin. J Clin Endocrinol Metab. 2001;86:2409–13.
28. Inoue M, Itabashi K, Nakano Y, Nakano Y, Tobe T. High-molecular-weight adiponectin and leptin levels in cord blood are associated with anthropometric measurements at birth. Horm Res. 2008;70:268–72.
29. Ertl T, Funke S, Sárkány I, Szabó I, Rascher W, Blum WF, et al. Postnatal changes of leptin levels in full-term and preterm neonates: their relation to intrauterine growth, gender and testosterone. Biol Neonate. 1999;75:167–76.
30. Kayemba-Kay's S, Geary MP, Pringle J, Rodeck CH, Kingdom JC, Hindmarsh PC. Gender, smoking during pregnancy and gestational age influence cord leptin concentrations in newborn infants. Eur J Endocrinol. 2008;159:217–24.
31. Pardo IMCG, Geloneze B, Tambascia MA, Pereira JL, Barros-Filho AA. Leptin as a marker of sexual dimorphism in newborn infants. J Pediatr. 2004;80:305–8.
32. Oliveira EFV, Gama SGN, Silva CMFP. Gravidez na adolescência e outros fatores de risco para mortalidade fetal e infantil no município do Rio de Janeiro, Brasil. Cad Saude Publica. 2010;26:567–78.
33. Nakano Y, Itabashi K, Maruyama T. Association between serum adipocytokine and cholesterol levels in cord blood. Pediatr Int. 2009;51:790–4.