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Original Article

Does Fetal Malnutrition Affect Ghrelin, Leptin, Adiponectin and Insulin Levels in the Cord Blood of Newborns?

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ABSTRACT

Aim: Fetal malnutrition is a condition characterized clinically by the inability of subcutaneous adipose tissue and muscle mass to reach the normal amount or by significant intrauterine loss. The major hormones regulating fetal growth, fetal energy metabolism and adipogenesis are insulin, leptin, ghrelin and adiponectin. Cholesterol and triglycerides are very important in fetal growth in the last period of pregnancy. In this study, it was aimed to compare the glucose, insulin, leptin, ghrelin, adiponectin, cholesterol and triglyceride levels in the cord blood of newborn babies with and without fetal malnutrition.

Materials and Methods: Term babies born in our hospital were included in this study. Babies with a Clinical Assessment of Nutritional Status of 24 or below were considered as cases with fetal malnutrition, and those over 24 were considered as cases without fetal malnutrition. Glucose, insulin, leptin, ghrelin, adiponectin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol and triglyceride levels were studied from blood samples taken from the umbilical cord after delivery.

Results: A total of 80 term newborn babies (40 babies with fetal malnutrition and 40 babies without fetal malnutrition) were included in this study. Birth weight, glucose and insulin values were found to be significantly lower in the group with fetal malnutrition ($p<0.001$; $p<0.001$; $p=0.047$, respectively), and adiponectin levels were found to be significantly higher ($p<0.001$).

Conclusion: In our study, adiponectin levels in cord blood were found to be high in infants with fetal malnutrition. Considering the anti-inflammatory role of adiponectin, high adiponectin levels in infants with fetal malnutrition may directly or indirectly reflect a protective mechanism.

Keywords: Fetal malnutrition, ghrelin, leptin, adiponectin, insulin

Introduction

Fetal malnutrition (FM) is characterized by the inability to attain optimal amounts of subcutaneous adipose tissue and muscle mass in fetus or by a significant intrauterine loss of them. FM along with its typical clinical features was first described by Scott and Usher (1) in 1964. The Clinical Assessment of Nutritional Status (CANSCORE) has been developed as a simple and quick method to identify FM. It can be used independently of current assessments based on population norms in term newborn infants (2). FM can occur at any birth weight. FM is the most common cause of intrauterine growth restriction (IUGR) (3).

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Fetal growth is a complex process regulated by genetics, maternal factors, the intrauterine environment, and maternal and fetal hormones. Insulin is one of the most important hormones involved in fetal growth. The main axis in regulation of fetal growth is glucose-insulin-insulin-like growth factor-1 (4). In many studies, the cord insulin level of infants with fetal growth restriction was significantly lower compared to those without fetal growth restriction (5,6).

Other hormones, such as leptin, ghrelin, and adiponectin, are the hormones involved in the growth and the regulation of energy, homeostasis and appetite during the fetal and early postnatal period. Plasma leptin concentrations reflect the overall amount of adipose tissue and are positively correlated with insulin resistance (7). Ghrelin increases body weight, secretion of growth hormone, creates a positive energy balance, diminishes energy expenditure and enhances lipid accumulation (8). Adiponectin modulates insulin action and has anti-atherogenic and anti-inflammatory effects. Adiponectin levels are inversely proportional to body fat content and negatively correlated with insulin resistance (9,10).

Apart from these hormones responsible for the growth of fetal adipose tissue, cholesterol and triglyceride with an indirect effect are also very important in the fetal growth. Although the pathogenesis of intrauterine growth retardation has not been elucidated precisely, it is known that metabolic changes in the mother contribute to this process. Cholesterol and triglycerides are also crucial in the growth of the fetus, especially during the third trimester of pregnancy (11). In this study, it was aimed to compare the glucose, insulin, leptin, ghrelin, adiponectin, cholesterol and triglyceride levels in cord blood of newborn infants with and without FM.

Materials and Methods

Patients

This study was approved by the Medical School Ethics Review Board (26.12.2018-20.478.486) and funded by the University Scientific Research Projects Office (Reference number: 2019-008). Term newborn infants (gestational age ≥38 weeks according to the last menstrual period) who were born alive in our hospital between May 2019 and October 2019 were included in this study. Multiple pregnancies, premature newborns (gestational age <38 weeks), stillbirths, mothers with pre-pregnancy diabetes, gestational diabetes, hypertension and those infants of mothers with premature rupture of membranes were excluded from this study. Informed consent was obtained from all patients included in this study. Between May 2019 and October 2019, 370 newborn babies were born term in our hospital. A total of 80 term newborn infants were included in this study. The newborn infants were examined, and their weight, height and head circumference measurements were made following delivery.

CANSCORE scoring method

The CANSCORE was calculated using the CANSCORE method (2) by the same pediatrician within the first 12-24 hours after delivery. Nine signs and symptoms are evaluated in the CANSCORE method (2). Scoring is performed by examining the infant's hair, cheek fullness, chin fat folds, subcutaneous fat tissue in the arms and legs, whether the skin is loose and easily grasped and pulled away, the appearance of the ribs and intercostal space, the skin and adipose tissue on the back, subcutaneous fat tissue in the abdomen, and the number and depth of skin folds in the gluteal region. In the CANSCORE method, a minimum of 1 (poor, severe FM) and a maximum of 4 (good, no malnutrition) points are given for each parameter. At the end of the evaluation, a minimum of 9 and a maximum of 36 points can be obtained. The cut-off value of the CANSCORE is 24.

Newborns with a CANSCORE of 24 or below are considered as cases with FM. Those with a CANSCORE greater than 24 are considered as those without FM. With regard to the weight percentile of the newborn infants, those with a birth weight below the 10th percentile were considered as SGA babies, those with a birth weight between the 10th and 90th percentiles as AGA babies, and those with a birth weight above the 90th percentile were considered as LGA babies. Ponderal index values were calculated by using the weight and height measurements of the newborns with SGA. Those with a Ponderal index of 2.25 or below were considered as asymmetrical SGA.

Blood samples

After the umbilical cord was clamped following delivery, blood samples were taken from the umbilical cord. Glucose, insulin, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HLD) cholesterol, very-low-density lipoprotein (VLDL) cholesterol, and triglyceride values were measured immediately. HOMA was calculated according to the formula: insulin (microU/L) x glucose (nmol/L)/22.5.

Another blood sample was centrifuged at 5,000 rpm for 10 minutes and the separated serum sample was stored

at -80 °C until leptin, adiponectin, and ghrelin levels were measured. After collecting all the blood samples, the ghrelin, leptin and adiponectin levels of the separated serum samples were measured using ELISA kits.

Statistical Analysis

Statistical analysis was performed using the "SPSS (Statistical Package for Social Sciences) 16.0 for Windows" program. T-test, chi-square test, One-Way ANOVA and Cohen's kappa coefficient methods were used to evaluate the data. A p-value less than 0.05 was considered as statistical significance.

Results

Eighty newborn infants, 40 with FM and 40 without FM, were included in this study. When the demographic characteristics of the infants were analyzed, the mean gestational age was 38.20±0.97 (38-41) weeks. Thirty-five (43.7%) of the infants were female and 45 (56.3%) were male. Mean birth weight was 3,316.18±445.75 gr (2,230-4,530), mean birth height was 47.66±1.65 cm (43-52), and mean head circumference was 34.70±1.67 cm (31-38.5). When the demographic characteristics of the 40 infants with and the 40 infants without FM were examined, statistically significant differences were found between their birth weight, birth head circumference, Ponderal index value, CANSCORE and birth weight according to gestational week (Table I).

With regard to the antenatal history of the FM and non-FM groups, it was noted that maternal age was similar in both groups. There were no statistically significant differences between the mothers' pre-pregnancy weight, post-pregnancy weight, height or body mass index. No significant differences were found between the education levels of the mothers, the age of the father, or the income levels of the family (Table II).

When the FM group and the non-FM group were compared, the glucose level in the cord blood of newborn infants was significantly lower in the FM group (p<0.001), and the insulin value was significantly lower in the FM group (p=0.047). There was no significant difference between the groups with regard to leptin and ghrelin levels. The adiponectin level was significantly lower (p<0.001) in the FM group. When the lipid profile of the cord blood of the newborns in the FM and non-FM groups was

Table I. Demographic characteristics of the groups with and without fetal malnutrition

	Fetal malnutrition (+) (n=40)	**Fetal malnutrition (-) (n=40)**	**p-value**
Sex (n, %) - Female - Male	 15 (37.5) 25 (62.5)	 20 (50) 20 (50)	0.184
Birth weight (mean ± SD) (gr)	3.127.62±368.14	3.504.75±440.48	**<0.001**
Birth height (mean ± SD) (cm)	47.45±1.84	47.87±1.41	0.252
Head circumference (mean ± SD) (cm)	34.26±1.64	35.13±1.60	**0.018**
Ponderal index (mean ± SD) [(g/cm^3) x 100]	2.92±0.30	3.18±0.37	**0.001**
Birth method (n, %) - SVD - C/S	 2 (5) 38 (95)	 1 (2.5) 39 (97.5)	0.500
Gestational age (mean ± SD) (week)	38.01±1.12	38.42±0.74	0.058
Gestational age according to ultrasound (mean ± SD) (week)	37.72±1.32	38.17±1.03	0.094
Intrauterine growth restriction (n, %)	4 (10)	3 (7.5%)	0.500
CANSCORE (mean ± SD)	21.20±5.52	29.70±3.79	**<0.001**
APGAR score (median, min.-max.) - 1st minute - 5th minute	 8 (6-9) 9 (8-10)	 8 (7-9) 9 (8-10)	 0.728 1.000
Birth weight according to gestational week (n, %) - SGA - AGA - LGA	 1 (2.5) 39 (97.5) 0 (0)	 0 (0) 33 (82.5) 7 (17.5)	**0.014**

SD: Standard deviation, min.: Minimum, max.: Maximum, CANSCORE: The Clinical Assessment of Nutritional Status, SVD: Spontaneous vaginal delivery, C/S: Caesarean section, SGA: Small for gestational age, AGA: Appropriate for gestational age, LGA: Large for gestational age

compared, no significant differences were found in terms of total cholesterol, LDL cholesterol, HDL cholesterol, VLDL cholesterol, or triglyceride levels (Table III).

Discussion

Even though it is generally accepted that fetal growth restriction poses an increased risk for perinatal morbidity and mortality, the definition of fetal growth restriction is still problematic. In order to identify FM, a simple and quick method has been developed which can be used independently of the current assessments made according to population norms in term newborns. This method is called CANSCORE. FM can occur at any birth weight.

The weight, height and head circumference of a newborn with FM may or may not be within normal limits (2). The cut-off value for the CANSCORE is 24. Infants with a CANSCORE of 24 or below are considered as cases with FM. In a study conducted by Metcoff (2), the prevalence of FM via the CANSCORE method was found to be 10.9%. In

Table II. Antenatal characteristics of the groups with and without fetal malnutrition

	Fetal malnutrition (+) (n=40)	**Fetal malnutrition (-) (n=40)**	**p-value**
Mother's age (mean ± SD)	30.75±5.15	30.00±4.51	0.491
Mother's pre-pregnancy weight (mean ± SD) (kg)	72.43±16.42	72.25±16.77	0.960
Mother's weight at the end of pregnancy (mean ± SD) (kg)	84.71±15.39	82.65±16.43	0.564
Mother's weight gain during pregnancy (mean ± SD) (kg)	12.27±4.85	10.42±5.30	0.108
Mother's height (mean ± SD) (cm)	162.65±5.82	160.42±6.21	0.102
Mother's body mass index (mean ± SD) (kg/cm^2)	27.35±6.13	28.07±6.81	0.621
Body mass index (n, %) - Below normal - Normal - Overweight - Obese	 1 (2.5) 18 (45) 9 (22.5) 12 (30)	 0 (0) 15 (37.5) 14 (35) 11 (27.5)	0.493
Mother's illiteracy (n, %)	5 (12.5)	3 (7.5)	0.506
Paternal age (mean ± SD)	33.65±5.27	33.87±4.71	0.841
Family income rate (mean ± SD) (Turkish Liras)	2.877.50±1.777.27	2.458.00±1.133.18	0.212

SD: Standard deviation

Table III. Mean glucose, insulin, HOMA, leptin, ghrelin, adiponectin and lipid profile values in cord blood of infants with and without fetal malnutrition

	Fetal malnutrition (+) (n=40) (Mean ± SD)	**Fetal malnutrition (-) (n=40) (Mean ± SD)**	**p-value**
Glucose (mg/dL)	51.20±13.02	66.70±19.58	**<0.001**
Insulin (mIU/mL)	5.44±3.80	10.28±14.65	**0.047**
HOMA	0.70±0.52	2.21±4.78	0.051
Leptin (ng/mL)	5.05±4.46	6.79±7.23	0.201
Ghrelin (ng/mL)	0.42±0.78	0.37±0.11	0.723
Adiponectin (ng/mL)	3.74±0.48	3.32±0.49	**<0.001**
Cholesterol (mg/dL)	66.60±22.23	64.92±21.28	0.732
LDL cholesterol (mg/dL)	29.30±16.73	28.77±18.09	0.893
HDL cholesterol (mg/dL)	31.10±8.86	30.30±7.52	0.665
VLDL cholesterol (mg/dL)	6.20±6.28	5.85±4.06	0.768
Triglyceride (mg/dL)	31.22±31.04	29.35±20.14	0.750

SD: Standard deviation, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very-low-density lipoprotein

a study conducted in our hospital in 2011, the frequency of FM in term newborns via the CANSCORE method was found to be 9.9% (12). In our study, the mean CANSCORE of the newborns with FM was 21.20±2.52 (16-24), and the mean CANSCORE of the newborns without FM was 29.70±3.79 (25-36). The CANSCORE was significantly higher in the group without FM ($p<0.001$). There was a statistically significant difference in birth weights according to the gestational age of the newborns in the groups with and without FM ($p=0.014$). Birth weight and birth head circumference were significantly lower in the group with FM than in the group without FM ($p<0.001$, $p=0.018$). There was no significant difference between average lengths at birth ($p=0.252$). The Ponderal index was significantly higher in the group without FM ($p=0.001$).

Fetal adipose tissue maturation in intrauterine life begins in the second trimester of pregnancy and further enhances during the third trimester. Fetal adipose tissue is necessary for lipid and more importantly, glucose metabolisms, as deficiency of adipose tissue leads to malnutrition and its excess results in obesity (13).

Adipokines are peptides produced mainly by adipose tissue. They play a critical role in energy homeostasis and metabolic regulation, and play a role in intrauterine growth (14). Fetal growth restriction hinders the proper formation of fat tissue in the fetus and can impair metabolic functions and endocrine secretions related to adipose tissue. In a rat model of FM, postnatal leptin administration reduced metabolic abnormalities in newborn rats (15). It has been reported that leptin levels in the cord blood are low in newborns with IUGR. These infants gain weight rapidly after birth and are prone to metabolic syndrome in adulthood (16,17). A positive correlation was found between fetal birth weight and fetal serum leptin levels. Leptin levels are lower in SGA infants (18).

Regardless of gestational age, birth weight is positively correlated with leptin levels (19). A positive correlation was found between serum leptin and glucose in term infants. It has been shown that there is a positive correlation between leptin and insulin by anthropometric measurements (20). In our study, blood glucose and insulin levels were significantly lower in the FM group, and leptin levels were reduced, although not significantly ($p<0.001$, $p=0.047$, $p=0.201$). In our study, insulin and leptin levels in the cord blood of newborns with FM were lower compared to those without FM and this finding is consistent with the literature.

Another peptide hormone which is crucial in fetal growth and reduces body weight and food intake due to its action as a leptin antagonist is ghrelin. Ghrelin increases body weight, enhances the secretion of growth hormones, produces a positive energy balance, reduces energy expenditure and promotes lipid accumulation (8). Regardless of gestational age, birth weight and total ghrelin exhibit a negative correlation (19). In our study, ghrelin levels were found to be high, although this was not significant in the FM group ($p=0.723$).

Another adipocytokine involved in intrauterine growth is adiponectin. Adiponectin is an indicator of insulin sensitivity and fatty acid oxidation (21). Therefore, decreased adiponectin levels may accompany increased insulin levels in infants with IUGR. It is thought that fetal maturation, hence the increase in fetal weight, affects cord blood adiponectin levels (22,23). SGA infants have reduced adiponectin levels. In one study, adiponectin levels in the cord blood of infants with IUGR were significantly lower than in the control group (24). In our study, unlike the findings reported in the literature, the level of adiponectin in the cord blood was significantly higher in those infants with FM compared to those without FM. Considering the anti-inflammatory role of adiponectin and pro-inflammatory role of leptin, we thought that low leptin levels and high adiponectin levels may directly or indirectly reflect a protective mechanism against chronic stress caused by FM.

Fetal adipose tissue is also essential for lipid metabolism because its deficiency leads to malnutrition (13). As Dios Garcia Diaz et al. (25) stated, the correlation of the lipoprotein profile in cord blood with fetal development parameters reveal conflicting results. While the relationship between lipid concentrations in cord blood and anthropometric measurements were found to be significant in certain studies, it was not reported to be significant in other studies (25,26). There were no significant differences in total cholesterol, LDL, HDL, VLDL cholesterol and triglyceride levels in cord blood, especially in normal birth weight infants with IUGR compared to healthy infants (27,28). In our study, there was no significant difference in lipid levels between the groups with and without FM. This may be due to the fact that the birth weights of the majority of infants in the with FM and without FM groups were compatible with their week of birth.

Study Limitations

The low number of cases and lack of long-term outcomes for patients are the limitations of this study.

Conclusion

The evaluation of fetal growth by birth weight alone can be misleading. Adipokines, particularly leptin and adiponectin, play a regulatory role in fetal growth. Given the anti-inflammatory role of adiponectin, high adiponectin levels in infants with FM may directly or indirectly reflect a protective mechanism.

Ethics

Ethics Committee Approval: This study was approved by the Medical School Ethics Review Board (26.12.2018-20.478.486) and funded by the University Scientific Research Projects Office (reference number: 2019-008).

Informed Consent: Informed consent was obtained from all patients included in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.T., B.E., F.T., E.Ö., Design: S.T., B.E., F.T., E.Ö., Data Collection and/or Processing: E.Ö., Analysis and/or Interpretation: B.E., F.T., Literature Search: S.T., B.E., F.T., E.Ö., Writing: S.T., B.E., F.T., E.Ö.

Conflict of Interest: The authors declared that there were no conflicts of interest.

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References

1. Scott KE, Usher R. Epiphyseal development in fetal malnutrition syndrome. N Engl J Med 1964; 270:822-4.
2. Metcoff J. Clinical assessment of nutritional status at birth. Fetal malnutrition and SGA are not synonymous. Pediatr Clin North Am 1994; 41:875-91.
3. Boedjang RF, Markum AH, Monintja HE, Aminullah A. Intrauterine growth chart in LBW Indonesian infants and some aspects of fetal malnutrition. Bulletin Int Pediatr Assoc 1979; 3:49.
4. Gluckman PD. Clinical review 68: The endocrine regulation of fetal growth in late gestation: the role of insulin-like growth factors. J Clin Endocrinol Metab 1995; 80:1047-50.
5. Godfrey KM, Hales CN, Osmond C, Barker DJ, Taylor KP. Relation of cord plasma concentrations of proinsulin, 32-33 split proinsulin, insulin and C-peptide to placental weight and the baby's size and proportions at birth. Early Hum Dev 1996; 46:129-40.
6. Verkauskiene R, Beltrand J, Claris O, et al. Impact of fetal growth restriction on body composition and hormonal status at birth in infants of small and appropriate weight for gestational age. Eur J Endocrinol 2007; 157:605-12.
7. Valle M, Gascón F, Martos R, Bermudo F, Ceballos P, Suanes A. Relationship between high plasma leptin concentrations and metabolic syndrome in obese pre-pubertal children. Int J Obes Relat Metab Disord 2003; 27:13-8.
8. Nakazato M, Murakami N, Date Y, et al. A role for ghrelin in the central regulation of feeding. Nature 2001; 409:194-8.
9. Whitehead JP, Richards AA, Hickman IJ, Macdonald GA, Prins JB. Adiponectin--a key adipokine in the metabolic syndrome. Diabetes Obes Metab 2006; 8:264-80.
10. Yildiz BO, Suchard MA, Wong ML, McCann SM, Licinio J. Alterations in the dynamics of circulating ghrelin, adiponectin, and leptin in human obesity. Proc Natl Acad Sci U S A 2004; 101:10434-9.
11. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab 2004; 89:2548-56.
12. Tanrıverdi S, Karaboğa B, Karaca Ö, Baytur Y. Prevalence of Fetal Malnutrition and Relationship Between Fetal Malnutrition and Fetal Acidemia. Turkiye Klinikleri J Pediatr 2012; 21:76-82.
13. Symonds ME, Mostyn A, Pearce S, Budge H, Stephenson T. Endocrine and nutritional regulation of fetal adipose tissue development. J Endocrinol 2003; 179:293-9.
14. Rosen ED, Spiegelman BM. Adipocytes as regulators of energy balance and glucose homeostasis. Nature 2006; 444:847-53.
15. Ellis PJ, Morris TJ, Skinner BM, et al. Thrifty metabolic programming in rats is induced by both maternal undernutrition and postnatal leptin treatment, but masked in the presence of both: implications for models of developmental programming. BMC Genomics 2014; 15:49.
16. Ozanne SE, Hales CN. Early programming of glucose-insulin metabolism. Trends Endocrinol Metab 2002; 13:368-73.
17. Tamura T, Goldenberg RL, Johnston KE, Cliver SP. Serum leptin concentrations during pregnancy and their relationship to fetal growth. Obstet Gynecol 1998; 91:389-95.
18. Valūniene M, Verkauskiene R, Boguszewski M, et al. Leptin levels at birth and in early postnatal life in small- and appropriate-for-gestational-age infants. Medicina (Kaunas) 2007; 43:784-91.
19. Martos-Moreno GA, Barrios V, Sáenz de Pipaón M, et al. Influence of prematurity and growth restriction on the adipokine profile, IGF1, and ghrelin levels in cord blood: relationship with glucose metabolism. Eur J Endocrinol 2009; 161:381-9.
20. Guzmán-Bárcenas J, Hernández JA, Arias-Martínez J, Baptista-González H, Ceballos-Reyes G, Irles C. Estimation of umbilical cord blood leptin and insulin based on anthropometric data by means of artificial neural network approach: identifying key maternal and neonatal factors. BMC Pregnancy Childbirth 2016; 16:179.
21. Rabe K, Lehrke M, Parhofer KG, Broedl UC. Adipokines and insulin resistance. Mol Med 2008; 14:741-51.
22. Crume TL, Scherzinger A, Stamm E, et al. The long-term impact of intrauterine growth restriction in a diverse U.S. cohort of children: the EPOCH study. Obesity (Silver Spring) 2014; 22:608-15.
23. Arita Y, Kihara S, Ouchi N, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun 1999; 257:79-83.
24. Aydin HI, Eser A, Kaygusuz I, et al. Adipokine, adropin and endothelin-1 levels in intrauterine growth restricted neonates and their mothers. J Perinat Med 2016; 44:669-76.
25. Dios Garcia Diaz Jd, Gaspar Blazquez MJ, Bienvenido Villalba M, Granizo Dominguez V, Jimenez Bustos JM. Relationship between lipoprotein profile in cord blood with obstetric variables and

anthropometry in newborns. Differ- ences related with sex. Clin InvestigArterioscler 2007; 19:215-22.

26. Soto N, Bazaes RA, Peña V, et al. Insulin sensitivity and secretion are related to catch-up growth in small-for-gestational-age infants at age 1 year: results from a prospective cohort. J Clin Endocrinol Metab 2003; 88:3645-50.

27. Ramy N, Zakaria M, El Kafoury M, Kamal M. Cord blood lipid profile in relation to anthropometric measures of newborns. Kasr Al Ainy Med J 2017; 23:54-8.

28. Rodie VA, Caslake MJ, Stewart F, et al. Fetal cord plasma lipoprotein status in uncomplicated human pregnancies and in pregnancies complicated by pre-eclampsia and intrauterine growth restriction. Atherosclerosis 2004; 176:181-7.