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Effects of nutrition education on adipocytokines levels in cord blood at birth

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Summary. *Background/aims:* Adipocytokines play a role in intrauterine growth but the effects of the nutrition education on adipocytokines and physical measurements at birth remains unclear. The aim of this study was to evaluate effects of nutrition education on adipocytokines levels in cord blood and physical measurements at birth. *Methods:* The present study involved 52 pregnant women who were in pregnancy followed up in Gazi University Medical School Hospital at Ankara, Turkey. They were randomly divided into two groups and experimental group involved in nutrition education. *Results:* There was a positive association between the cord blood leptin values of the both groups. Nutrition education had no significant effect on cord blood adiponectin, visfatin and IL-6 values of the newborns. Also there was not a significant difference between the average values of weight and the head circumference of newborns in both groups. In experimental group, the average birth length was observed to be higher than that of control group. *Conclusion:* Nutrition education might improve leptin levels of the newborns in the experimental group. In the lights of these results, it may be suggested that higher cord blood leptin levels could play an important role in higher birth length values of the newborns.

Key words: nutrition education, pregnancy, adipocytokines, newborns, anthropometry, birth

Introduction

Pregnancy is an occasion when women become more aware of the importance of healthy nutrition. A healthy and balanced "diet" during pregnancy is one of the most significant components affecting both the health of the mother and the health of the fetus. Since it is essential for a better pregnancy outcome pregnant women should receive nutrition education from their healthcare professionals during pregnancy. Nutrition education programmes are important as enhancing subject dietary intakes by promoting behavioral changes such as food choice and cooking ability. The maternal diet must provide sufficient energy and nutrients for the mother's usual requirements and the needs of the growing fetus (1-4). The prenatal life is a time of rapid cellular growth and replication and of functional maturation of organs in the intrauterine milieu. In pregnancy physiological adaptations are aimed to facilitate delivery of nutrients to the fetus. Since the discovery of adipocyte-derived hormones, commonly called adipocytokines, the adipose tissue is no longer considered an inactive fat store tissue, but an endocrine organ, secreting a variety of biological molecules, which regulate energy homeostasis as well as metabolism and inflammation in pregnant and non-pregnant women. In addition, adipocytokines have been recently implicated in fetal growth (5,6). Fetal growth is governed by multiple factors.

In pregnancy, adiponectin, leptin, visfatin and interleukin-6 (IL-6) like adipose tissue markers affect intrauterine metabolism (7,8). Adiponectin is an adipocyte-secreted hormone that modulates a number of metabolic processes, including glucose regulation and fatty-acid oxidation, and has an insulin-sensitizing effect. The umbilical cord blood adiponectin levels found to be positively associated with birth weight and fat mass. In addition to adiponectin, another adipocytokine, leptin is also found to be related to other physiological conditions beyond appetite control and obesity. Leptin has recently been proposed as a biomarker of fetal adiposity and provide a biological link for the fetal programming of later adult metabolic health. Adiponectin and leptin are present in cord blood and the positive correlation of their concentrations with neonatal birth weight as well as the high production of these adipokines may play important roles in fetal development (9-11). Visfatin is a protein that is produced in adipose tissue. Both tissue and plasma levels of visfatin increase in obesity. Moreover, circulating visfatin concentrations were shown to increase in hyperglycemia. It has insulin-mimetic effects and lowers plasma glucose levels (12,13). Cord blood IL-6 levels describe the intensity of the fetal inflammatory response. It has recently been shown that cord blood levels of IL-6 is of fetal origin and do not reflect maternal or placental cytokine production (14,15).

The effects of nutrition education on adipocytokines and physical measurements at birth remains unclear. The aim of this study was to evaluate effects of nutrition education on adipocytokines levels in cord blood and physical measurements at birth.

Methods

This was a randomized controlled trial conducted at Gazi University Medical School Hospital at Ankara, Turkey. 96 pregnant women who were in pregnancy followed up in Department of Gynecology and Obstetrics of Gazi University Medical School Hospital were assessed for eligibility. The mothers whose pregnancies are not older than 8 weeks, who have no diabetes, hypertension, acute or chronic diseases, who does not smoke, use alcohol or drugs were included in the research. Of the 32 women who met the inclusion criteria but refused to participate in this study. On the other hand 12 women had chosen to give birth in other hospitals or obstetrics clinics. In total, 52 pregnant women were randomized to the study. They were randomly divided into two groups: 26 and 26 pregnant women were included in the experimental and control groups, respectively. All the pregnant women were Turkish and they didn't have a migration background. In addition, they had an educational level of high school or higher. All women received oral and written information and signed an informed consent before entering the study. The control group did not receive dietary advice. Experimental group received dietary advice. The first study visit took place during the first trimester (pregnancy weeks 8–12). Follow-ups were done in the second trimester (pregnancy weeks 24–26) and the third trimester (pregnancy weeks 35–37).

Dietary advice was provided by trained dietitians throughout face to face interviews and dietitians followed up of the pregnant women during their pregnancy. Newborn infants born in Gazi University Medical School Hospital between October 2010 and March 2011 by normal, vaginal delivery and spontaneous were enrolled in this study. Newborns born with infection, thyroid, bone, renal, diabetes and gastrointestinal disorders were excluded. This study includes all births from 37 to 42 weeks of gestation. After birth, totally cord blood of 52 infants of mothers from both groups were taken and information related to height, weight and head circumferences of the infants were recorded.

All woman participants gave informed consent for themselves and their infants. The study was approved by the Gazi University Medical Faculty Ethic Commitee was received and informed consent was obtained before the blood samples were taken. The study was carried out in compliance with the Helsinki Declaration. This work was supported by Gazi University, Scientific Research Projects Committee '[08/2010-09]' (Figure 1).

Dietary Intervention

Participants received dietary counseling on the day of their visit to Gazi University Hospital. Dietary advice focused on enhancing the quality of the diet, by educating women on which foods and what quantities they need to consume in order to achieve the dietary intake. The recommended energy intake for pregnant women is: no additional energy requirement in the first trimester, 340 kilocalories (kcal) extra energy per day for the

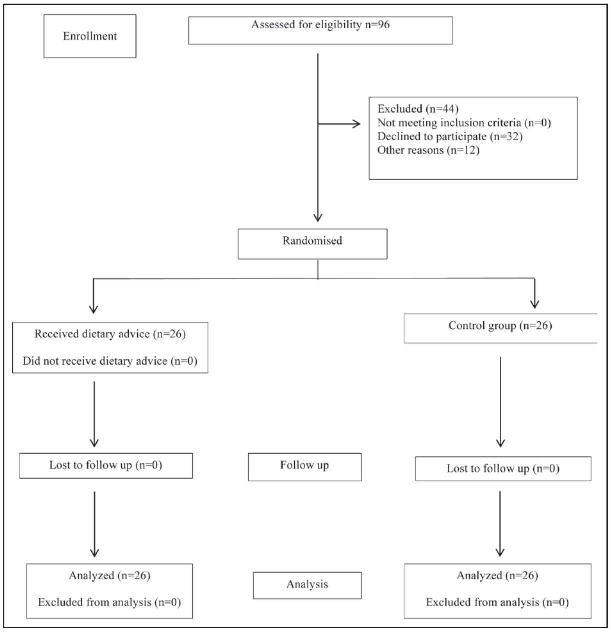

Figure 1. Participant flow in CONSORT-recommended form.

second trimester and 450 kcal extra energy per day for the third trimester. The recommended daily protein intake in the first trimester is 45 g per day (0.75 g/kg/day). In the second and third trimesters the required protein intake for pregnant women is 60 g per day (1.00 g/kg/day). They were advised to consume two meals of fish per week. The recommended carbohydrate intake is 170 g and dietary fibre intake is 20 g per day. Dietary intake of linoleic acid is 10 g per day, 1 g per day a-linolenic acid, and 110 mg per day total eicosapentaenoic acid, docosahexaenoic acid. The recommended daily intake of milk or yogurt is 500 g. In addition to these, all participants received advice on dietary sources of iron, calcium, zinc, copper, selenium, magnesium and iodine.

The participants were encouraged to consume of variety of fruits and vegetables each day by reducing their intake of sugar sweetened soft drinks and fruit juices. Diet quality was individually adjusted as needed, and counseling was also given on fat quality, food frequency, fibre intake, and nutrient density according to the Dietary Guidelines of Turkish Ministry of Health. After their first visit, women were repeatedly (twice a week) called by telephone to remind them of the recommendations and were followed-up the second and third trimesters.

Anthropometric Measurements

All the measurements were done while the newborn has been lying supine on the examining table and on the right side of its body. Each baby was measured 30 minutes after being feed. Birth weight (gm), length (cm), head and circumference measurements (cm) were recorded. Newborn anthropometric measurements were obtained within 24 hours of delivery.

Biochemical Analysis

Cord blood which was placed into biochemical tubes for the analysis were centrifuged for 5 minutes at 3000 RPM and plasma and serum were separated and placed in Eppendorf tubes and were kept at -80 ° C until the day of analysis in the Department of Biochemistry. SIGMA (6K15) laboratory type centrifuge and BIOTEK (microplate reader/Snergy HT) ELISA (Enzyme-Linked Immuno Sorbent Assay) Analyzer were used for analysis of the cord blood samples. Determination of leptin and IL-6 were performed using Immunoenzymetric assay kits (DIAsource - Louvain-la-Neuve, Belgium), while adiponectin levels were measured with commercial ELISA kit (enzyme immunoassay kit - Biovendor (Brno, Czech Republic). Visfatin levels were measured by Visfatin C-Terminal (Human) Enzyme Immunoassay Kit (Phoenix Pharmaceuticals, CA, USA), according to the manufacturer's instructions.

Statistical Analysis

Statistical analysis was performed with SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Clinical and anthropometrical data of the study populations are given as means ± SD. To check the normality of the data distribution Kolmogorov-Smirnov test and Shapiro-Wilk test was performed. Differences in the means of variables were tested using both parametric and nonparametric tests depending on the distribution of the variables.

In order to detect the differences between the groups Paired samples t-test and Mann-Whitney U test were used. For all statistical analysis p-values below 0.05 and 0.01 were considered significant.

Results

The baseline characteristics and measurements are presented in Table 1. The mean maternal age of women were 29 ± 2.9 (years) in the control and 29 ± 3.1 (years) in the experimental group. Maternal Body Mass Index (BMI) was calculated during the first trimester (pregnancy weeks 8–12). Follow-ups were done in the second trimester (pregnancy weeks 24–26) and the third trimester (pregnancy weeks 35–37).

Mean birthweight, length and head circumference values of the newborns in the control group were 3590 ± 322 gm, 52 ± 2.1 cm and 34.8 ± 1.2 cm respectively. While in the experimental group, mean birthweight, length and head circumference values of the newborns were 3870 ± 319 gm, 53 ± 3.3 cm and 33.6 ± 1.8 cm respectively (Table 1).

Table 2 shows that, cord blood adiponectin average values of the experimental group (31,446 ± 1,6446 µg/ml) were higher than average values of the control group (30,023 ± 1,6007 µg/ml). However, there was no significant difference between the cord blood adiponectin values of the experimental and control groups (p>0.05). Average leptin values determined in the experimental group (4,3227 ± 0,9262 ng/mL) were higher than the control group values (2,6881 ± 0,56056 ng/mL). There was a positive association between the cord blood leptin values of the experimental and control groups (p<0,05). Average visfatin values of the experimental group (4,031±0,2939 ng/ml) were slightly lower than the values of the control group (4,123 ± 0,3321 ng/ml). But, there was no significant association between the cord blood visfatin values of the experimental and control groups (p>0,05). IL-6 average values (9,127 ± 1,3408 pg/ml) of the experimental group were lower than the average values of the control group (23,538 ± 16,397 pg/ml). There was no significant association between the cord blood IL-6 values of the control and experimental groups (p>0,05). Except for the leptin values, nutrition education during pregnancy had no significant effect on cord blood adiponectin, visfatin and IL-6 values of the newborns.

Table 1. Maternal and infant characteristics

Characteristics	Control (n=26)	Experimental (n=26)
Maternal age (years)	29 ± 2.9	29 ± 3.1
Early-pregnancy BMI (kg/m2)	23.1 ± 3.8	23.0 ± 4.2
Mid-pregnancy BMI (kg/m2)	25.6 ± 3.9	25.8 ± 3.8
Late-pregnancy BMI (kg/m2)	27.9 ± 4.4	28.1 ± 4.2
Parity		
0	12 ± 3	11 ± 2
1	10 ± 3	11 ± 3
≥2	4 ± 4	4 ± 2
Infants		
Female/male	11/15	14/12
Birthweight (gm)	3590 ± 322	3870 ± 319
Length (cm)	52 ± 2.1	53 ± 3.3
Head circumference (cm)	34.8 ± 1.2	33.6 ± 1.8
Gestational age at delivery (weeks)	38.1 ± 2.4	39.0 ± 2.1

Data are medians (SDs).

In Table 3, it is seen that the average birth weights of newborns in the experimental group (3295,63 ± 62,492 gm) was slightly higher than the average birth weights of newborns in the control group (3230,02 ± 65,232 gm). The results indicate that there was not a significant difference (p>0,05) between the average weights of newborns in control and experimental groups. In the experimental group, the average birth length (49,771 ± 0,2879 cm) was observed to be higher than that of control group (48,604 ± 0,2675 cm). In other words, on average, the newborns in the experimental group were taller than the newborns in the control group. The statistical analyses proved that there was a significant difference (p<0,01) between the birth lengths of the newborns in the experimental group and those in the control group.

The head circumference average of newborns in the experimental group (34,156 ± 0,1349 cm) was seen to be higher than the average head circumference measured in the control group (33,781 ± 0,2068 cm). However, statistical analyses showed that the head circumference rates did not differ significantly (p>0,05) between control and experimental groups.

Table 2. Comparison of cord blood adipokines values between the groups

	Groups	N	X	Std. Error	min	max	p
	Experimental	26	31,446	1,6446	17,4	45,5	
Adiponectin, (µg/ml)	Control	26	30,023	1,6007	15,5	45,5	,538
	Total	52	30,735	1,1406	15,5	45,5	
	Experimental	26	4,3227	,69262	,79	13,00	
Leptin, (ng/mL)	Control	26	2,6881	,56056	,60	14,30	,035*
	Total	52	3,5054	,45573	,60	14,30	
	Experimental	26	4,031	,2939	2,6	8,1	
Visfatin, (ng/ml)	Control	26	4,123	,3321	2,6	9,6	,811
	Total	52	4,077	,2197	2,6	9,6	
	Experimental	26	9,127	1,3408	1,9	27,8	
IL-6, (pg/ml)	Control	26	23,538	16,397	2,4	433,0	,735
	Total	52	16,333	8,2072	1,9	433,0	

*Mann-Whitney U test was conducted. *p<0,05*

Table 3. Comparison of anthropometric measurements between the groups

	Groups	N	X	Std. Error	min	max	p
	Experimental	26	3295,63	62,492	2410	4180	
Birth weight (gm)	Control	26	3230,02	65,232	2210	4030	,470
	Total	52	3262,82	45,055	2210	4180	
	Experimental	26	49,771	,2879	46,0	53,0	
Birth Length (cm)	Control	26	48,604	,2675	44,0	52,0	,004**
	Total	52	49,188	,2044	44,0	53,0	
	Experimental	26	34,156	,1349	32,5	36,5	
Head circumference (cm)	Control	26	33,781	,2068	30,5	37,0	,132
	Total	52	33,969	,1243	30,5	37,0	

*Mann-Whitney U test was conducted. **p<0,001; *p<0,05*

Discussion

Pregnancy is characterized by endocrine and metabolic maternal adaptations including increase in weight, body fat mass, and insulin resistance. These changes are physiological adaptations necessary to meet the energy demand of the fetus and prepare the maternal organism for delivery and lactation. A group of cytokines, collectively known as adipocytokines, have endocrine and paracrine effects. The most studied adipokines are leptin, adiponectin, resistin, IL-6 and visfatin. Markedly high levels of adipokines have been detected in umbilical plasma, hence, suggesting a possible role on fetal development and metabolism (16).

Good nutrition during pregnancy is one of the most significant components affecting both the health of the mother and the health and development of their unborn babies. Poor maternal nutrition has been linked with poor infant outcomes. These include inadequate development, low birth weight and an increased risk preterm birth or even miscarriage. Also poor maternal nutrition associated with maternal excess weight gain, pre-eclampsia, increased risk of developing chronic diseases (17).

Systematic review and meta-analysis of 34 studies providing nutrition education with and without nutrition support in the form of food baskets, food supplements or micronutrient supplements found that nutrition education improved gestational weight gain, reduced the risk of anemia in late pregnancy, increased birth weight and lowered the risk of preterm delivery [18]. According to Ota et al., nutrition advice improves nutrient intakes during pregnancy, reduces the risk of preterm birth by 54% and increases head circumference at birth [19]. It has been demonstrated that cord blood concentrations of leptin and adiponectin are associated with body mass index and adiposity in neonates (20).

In 2004, Tsai et al. examined the relationships between cord plasma concentrations of adiponectin and leptin in healthy term neonates. They found that, adiponectin and leptin levels were positively correlated with birthweight and adiposity. They suggested that these adipocytokines positively associated with intrauterine growth [21]. In 2009, Cekmez et al. examined the relationship between adiponectin, visfatin, insulin and birthweight at birth in healthy term infants. They found that, cord plasma adiponectin and visfatin levels were positively correlated with birthweight. They also suggested that, adiponectin and visfatin might be involved in regulating fetal growth (22). Conversely we did not find a significant association between adiponectin and visfatin values of the both groups.

IL-6 during pregnancy mainly due to placental production and has been related to pregnancy-associated insulin resistance. Cord blood IL-6 could be related with hypoxia, nutrient deficiency and early-onset neonatal sepsis (23-25). Moreover, high cord blood IL-6 concentrations in premature infants with fetal inflammatory response syndrome were found to be predictive for respiratory distress syndrome and death (26). In our study, cord blood IL-6 levels were found to be lower in experimental group with respect to control group. Nutrition education during pregnancy might be responsible for low IL-6 levels in the cord blood. In 2011, Nakano et al. conducted a study on 52 Japanese newborns. They found a positive relationship between cord plasma leptin levels and anthropometry. Higher levels of leptin appeared to correlate with an increased amount of fats accumulated in the fetus, resulting in higher BMI. However they did not find any association between cord adiponectin levels and anthropometry. They concluded that, leptin was one of the key hormones for controlling fetal lipid metabolism in addition to fetal growth (27). In another study, Kahveci et al. found a positive correlation between newborn leptin levels and anthropometrics. They suggested that leptin could play a role in newborn growth and development (28).

In our study, we found a positive association between leptin and birth length levels of the newborns whose mother received nutrition education during their pregnancy. Accordingly, it can be said that the nutrition education during pregnancy is effective on leptin values and leptin plays an important role in the process of fetal growth. A major limitation of this current study is the relatively small sample size. The relatively small sample size decreased the ability to detect significant differences across groups.

Conclusion

In conclusion, we showed that cord plasma leptin and birth length values of the newborns in the experimental group were significantly higher than the control group. Taken together these findings suggest that nutrition education might improve leptin levels of the newborns in the experimental group. In the lights of these results, it may be suggested that higher cord blood leptin levels could play an important role in higher birth length values of the newborns. Further studies are needed to better understand whether these adipocytokines are differentially regulated in the course of pregnancy.

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