

## Role of Leptin in Growth and Adiposity in Early Infancy: Impact of Nutritional Pattern

A Çamurdan Duyan, F Sahin, MO Çamurdan, \*A Bideci and P. Cinaz

From the Department of Social Pediatrics and \*Department of Pediatric Endocrinology, Gazi University,  
Faculty of Medicine, Ankara, Turkey.

Correspondence to: Çamurdan Duyan A, Devlet mahallesi, Devrimler caddesi, 359. sokak, Yesiloz sitesi II/5,  
06374, Eryaman Ankara, Turkey. E-mail: aysucamurdan@yahoo.com.

Manuscript received: January 18, 2007; Initial review completed: May 9, 2007;  
Revision accepted: June 5, 2007.

*This study was planned to investigate leptin levels under different models of nutrition and their relation with anthropometric parameters in early infancy. Sixty four infants (28 exclusively breast-fed, 15 exclusively formula-fed and 21 mixed-fed), aged 4 months were included and their leptin, insulin-like growth factor-I (IGF-I), and IGF binding protein-3 (IGFBP-3) levels were measured. Leptin, IGF-I and IGFBP-3 levels of the three groups were not statistically different ( $P>0.05$ ). The results of our study questions the role of leptin as a link between nutritional pattern and adiposity-growth in early infancy.*

**Key words:** Adiposity, Children, Leptin.

Obesity is a leading cause of morbidity and mortality(1,2). Therefore, identification of factors leading to it is particularly attractive. The relationship of early introduction of solid foods and/or formula with adiposity and the protective effect of breastfeeding proves that this area needs considerable attention(3,4). Although leptin is widely studied in children and adult subjects and its role in adiposity and energy balance is almost clear, the function of leptin in infants is still an area to be searched intensively. It is not clearly understood whether circulating level of leptin is the cause or the consequence of many physiological conditions in infants(6,7). This study, was planned to investigate the role of leptin on anthropometric parameters in infants with different feeding patterns.

### Subjects and Methods

All healthy, term infants, who attended to well child clinics for the 4th month visit between June 2004 and December 2004 were included in the study. The infants were divided into 3 groups according to their feeding patterns.

#### *Exclusively breast-fed*

Infants who were fed by breast milk without receiving any formula or complementary foods.

#### *Exclusively formula-fed*

Infants who were fed exclusively by formula

since their birth or for at least 2 months before current visit, due to the factors like maternal illnesses or drugs that are contraindicated for breastfeeding or unwillingness of mother to breast feed, *etc.*

#### *Mixed-fed*

Infants who are fed with both breast milk and formula.

Preterm infants or infants who were small for gestational age and infants with diseases severe enough to be hospitalized and infants with feeding patterns different from those described above (having complementary foods, *etc.*) were excluded.

Serum leptin, insulin-like growth factor-I (IGF-I), and IGF binding protein-3 (IGFBP-3) levels were measured from the samples taken after at least 3 hours fasting. Samples were centrifuged and stored at  $-70^{\circ}\text{C}$  until they were analyzed. Serum leptin levels were measured using RIA (Phoenix Pharmaceuticals Inc., Belmont, USA), while serum IGF-I and IGFBP-3 levels were measured using IRMA (with DSL-5600 and DSL-6600 kits respectively) methods.

The study was approved by the institutional ethical committee.

Statistical analyses were performed by SPSS version 12. Chi-square and Kruskal-Wallis tests

were used in order to compare groups and Pearson correlation analyses were used to determine correlations between parameters after performing log-transformation for those which did not show normal distribution according to one-sample Kolmogorov-Smirnov test.

## Results

A total of 64 infants were included in the study. There were 28 infants in the exclusively breast-fed group, 15 in the exclusively formula-fed group and 21 in the mixed-fed group. Gender and anthropometric parameters of the infants are shown in *Table I*. No difference was found among the three groups according to sex and anthropometric parameters ( $P > 0.05$ ). Mean leptin, IGF-I and IGFBP-3 levels are provided in *Table II*. These levels were similar in the three groups ( $P > 0.05$ ). There were no correlations between serum leptin levels and other parameters considered in the study (including the timing of formula and duration of exclusive breastfeeding) when the study group was taken as a whole or the groups were analyzed separately.

There were no differences between male and

female infants and between groups by means of leptin, IGF-I, IGFBP-3 and anthropometric parameters.

## Discussion

Nutritional pattern, and the hormone closely related to it, namely leptin are among the important factors considered to be the determinants of adiposity. There are studies postulating that the higher leptin concentration associated with greater body fatness early in postnatal life programs the leptin dependent feedback loop such that the regulation of body fat is less sensitive to leptin in later life(8).

Nutritional pattern is proven to be the contributing factor leading to adiposity later in life. Breastfeeding plays a protective, while early introduction of complementary foods and/or formula play a contributing role in adiposity(4). There are studies that show a link between nutritional pattern in early childhood and leptin levels later in life, especially in the adolescent period(8). Here the question that has been the most important aim of our study arises; is there a link between nutritional pattern and the postulated

**TABLE I**—Sex and Anthropometric Parameters of the Groups\*

	Breast-fed Group (n=28)	Formula-fed group (n=15)	Mixed-fed group (n=21)	P
Sex (male/female)	16/12	10/5	12/9	>0.05
Weight (kg)	7.3±0.7	7.5±0.9	7.5±0.8	>0.05
Height (cm)	65.2±2.7	67.1±3.8	65.9±2.7	>0.05
Body mass index (kg/m <sup>2</sup> )	17.3±1.5	16.6±1.4	17.3±1.7	>0.05
Birth weight (kg)	3.4±0.4	3.3±0.6	3.4±0.3	>0.05
Birth height (cm)	50.9±1.8	50.2±2.6	50.4±1.7	>0.05

\* Data are given as; mean ± SD.

**TABLE II**—Serum Leptin, IGF-I and IGFBP-3 Values in Groups\*

	Breast-fed Group (n=28)	Formula-fed group (n=15)	Mixed-fed group (n=21)	P
Log Leptin (pg/mL)	0.80±0.22	0.78±0.32	0.76±0.19	>0.05
IGF-I (ng/mL)	7.6±1.7	7.5±1.5	8.0±2.3	>0.05
IGFBP-3 (ng/mL)	1780.5±237.0	1992.8±358.6	1997.5±537.5	>0.05

\*: Data are given as; mean ± SD.

**What is Already Known?**

- There are studies that show a link between nutritional pattern in early childhood and leptin levels later in life.

**What this study adds?**

- Leptin levels were similar in exclusively breast-fed, exclusively formula-fed and mixed-fed groups. We think that the effect of breast or formula feeding on growth and adiposity is not brought via changes in leptin levels, at least in early infancy.

higher leptin levels in early infancy? In our study exclusively breast-fed, exclusively formula-fed and mixed-fed groups had similar leptin levels. Besides, leptin levels had no correlation with neither weight nor BMI when groups were considered separately or as a whole. These findings suggest that the effect of breast or formula feeding on adiposity is not brought via changes in leptin levels, at least in early infancy. There are other studies in favor of our suggestion in which no differences in plasma leptin and leptin/BMI between breast fed and formula fed infants at 1 and 4 months of age and no relation of leptin levels and adiposity during infancy could be shown(6,9). This relationship could not be observed even in the studies in which breast fed infants had higher leptin levels(10,11). Our data surely does not eliminate the postulated “programming” process, extended time may be needed for this process to emerge. There may be other factors linked to nutritional pattern that lead to adiposity, such as insulin, as postulated with another study(12). The protective effect of breast feeding may also be a direct consequence of biologically active hormones and factors that are present in human milk which may modulate mediators such as epidermal growth factor and tumor necrosis factor alpha, which are known to inhibit adipocyte differentiation *in vitro*(13).

Another finding in our study was that serum leptin levels did not have any correlations with growth parameters, IGF-I and IGFBP-3. This may suggest that although leptin is proven to be effective in growth in utero, this effect does not take place in postnatal life, at least in early infancy(14,15). Overall, the results of our study questions the role of leptin as a link between nutritional pattern and childhood adiposity and its role in early childhood growth. Extended prospective studies, considering wider range of age groups are needed in order to

overrule or support these questions.

*Contributor's Credits:* ACD was involved in designing the study, data collection and preparation of the manuscript. She will act as guarantor of the study. FS was involved in designing the study, data collection and has reviewed the written manuscript. MOC collected and analyzed the data. AB was involved in designing the study. PC was involved in planning the study and revising it critically for content and final approval of the version to be published

*Source of funding:* Gazi University Research Fund.

*Competing interests:* None stated.

**REFERENCES**

1. Strauss RS, Pollack HA. Epidemic increase in childhood overweight, 1986-1998. *JAMA* 2001; 286: 2845-2848.
2. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA* 2002; 288: 1728-1732.
3. Wilson AC, Forsyth JS, Greene SA, Irvine L, Hau C, Howie PW. Relation of infant diet to childhood health: seven year follow up of cohort of children in Dundee infant feeding study. *BMJ* 1998; 316: 21-25.
4. Von Kries R, Koletzko B, Sauerwald T, von Mutius E, Barnert D, Grunert V, *et al.* Breast feeding and adiposity: cross sectional study. *BMJ* 1999; 319: 147-150.
5. Salbe AD, Nicolson M, Ravussin E. Total energy expenditure and the level of physical activity correlate with plasma leptin concentrations in five-year-old children. *J Clin Invest* 1997; 99: 592-595.
6. Lonnerdal B, Havel PJ. Serum leptin concentrations in infants: Effects of diet, sex, and adiposity. *Am J Clin Nutr* 2000; 72: 484-489.
7. Nagy TR, Gower BA, Trowbridge CA, Dezenberg C, Shewchuk RM, Goran MI. Effects of gender, ethnicity, body composition, and fat distribution on serum leptin concentrations in children. *J Clin Endocrinol Metab* 1997; 82: 2148-2152.

SHORT COMMUNICATIONS

8. Singhal A, Farooqi IS, O'Rahilly S, Cole TJ, Fewtrell M, Lucas A. Early nutrition and leptin concentrations in later life. *Am J Clin Nutr* 2002; 75: 993-699.
  9. Uysal FK, Onal EE, Aral YZ, Adam B, Dilmen U, Ardicolu Y. Breast milk leptin: Its relationship to maternal and infant adiposity. *Clin Nutr* 2002; 21: 157-160.
  10. Savino F, Costamagna M, Prino A, Oggero R, Silvestro L. Leptin levels in breast-fed and formula-fed infants. *Acta Paediatr* 2002; 91:897-902.
  11. Savino F, Nanni GE, Maccario S, Costamagna M, Oggero R, Silvestro L. Breast-fed infants have higher leptin values than formula-fed infants in the first four months of life. *J Pediatr Endocrinol Metab* 2004; 17:1527-1532.
  12. Lucas A, Sarson DL, Blackburn AM, Adrian TE, Aynsley-Green A, Bloom SR. Breast vs bottle: endocrine responses are different with formula feeding. *Lancet* 1980; 1: 1267-1269.
  13. Hauner H, Rohrig K, Petruschke T. Effects of epidermal growth factor (EGF), platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) on human adipocyte development and function. *Eur J Clin Invest* 1995; 25: 90-96.
  14. Schubring C, Siebler T, Kratzsch J, Englaro P, Blum WF, Triep K, *et al.* Leptin serum concentrations in healthy neonates within the first week of life: relation to insulin and growth hormone levels, skinfold thickness, body mass index and weight. *Clin Endocrinol (Oxf)* 1999; 51: 199-204.
  15. Matsuda J, Yokota I, Iida M, Murakami T, Yamada M, Saijo T, *et al.* Dynamic changes in serum leptin concentrations during the fetal and neonatal periods. *Pediatr Res* 1999; 45: 71-75.
-