RELATIONSHIP OF BREAST MILK LEPTIN WITH MATERNAL AND INFANT ADIPOSITY

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Abstract

INTRODUCTION: Leptin - the product of the obese gene (ob) - is synthesized by adipose tissue and contributes to the regulation of energy homeostasis and food intake. Recently, immunoreactive leptin was reported to be present in human milk. The aim of this study was to determine any possible link between breast milk leptin concentrations and adiposity in exclusively breast-fed infants.

METHODS: 130 healthy, exclusively breast-fed infants beyond neonatal period and their mothers were included in the study. Infants whose weight for age was above the 75th, and between 25th and 75th percentiles were defined as obese (n=65) and non-obese (n=65), respectively. Anthropometric measurements of infants and mothers were also made and breast milk samples were analyzed for leptin.

RESULTS: There was no significant difference between breast milk leptin concentrations of mothers of obese and non-obese infants. Breast milk leptin concentrations significantly correlated with mothers' body mass index ($r=0.54$, $P<0.001$) and weight ($r=0.46$, $P<0.001$). There was no significant correlation between breast milk leptin concentration and weight of infants.

CONCLUSIONS: Leptin concentrations of human milk are not different in the mothers of obese and non-obese infants. Our findings suggest that milk-borne leptin has no significant effect on adiposity during infancy.

Key Words: Breast milk, leptin, infant, adiposity.

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Introduction

Leptin - the product of the obese gene (ob) - is synthesized by adipose tissue and contributes to the regulation of food intake and energy metabolism.[1]

In rodents and humans, plasma concentrations of leptin highly correlate with adiposity in adults[2,3] and children[4,5] and are markedly elevated in obese individuals,[6] suggesting more intensive endogenous leptin production.[7]

It is believed that leptin is integral in the feedback loop from adipose stores to the hypothalamus, because leptin administration decreases food intake in rodents and non-human primates; in addition, it increases energy expenditure in mice and activates the sympathetic nervous system.[8,9]

Immunoreactive leptin detected in human infant cord blood[10] is produced by the placenta.[11] Human milk contains bioactive leptin which may play an important role in neonatal health and development.[11]

Leptin concentrations in milk were lower than in plasma and correlated with maternal body fat,[12,13] hence raising the possibility that milk leptin may have an effect on infant growth and metabolism.[14,15]

The principal objective of this study was to determine if breast milk leptin concentration is related to adiposity in exclusively breast-fed infants.

Materials and methods

The study population consisted of 130 exclusively breast-fed infants beyond neonatal period admitted to the South Health Center of Tehran University of Medical Sciences to receive Primary Health Care (PHC) services; the infants' mothers were also enrolled in the study.

The infants were divided into two groups. Group I included infants whose weight for age was above the 75th percentile (n=65) and were defined as obese.

Group II consisted of 65 non-obese randomly selected infants, whose weight was between the 20th and 75th percentiles on the growth charts from CDC 2000 (Center for Disease Control and Prevention) standards.

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All of the infants were healthy. Mothers' weight was measured using a Seca scale; length (±0.1 cm) was measured using a body-length measurer by pediatric nurses who were not aware of the study.

Breast milk was collected from mothers with the aid of nurses after feeding the baby in the morning between 9 and 11 AM. Body Mass Index (BMI) of mothers was calculated as weight in kilograms divided by the square of height in meters. Women using any type of medication were excluded from the study.

Milk samples were stored at -20º C before being assayed. Samples were kept in refrigerator overnight and were ultracentrifuged at 15000 rpm* for 10 minutes at +4º C to separate milk fat. The fat layer was removed using a spatula and liquid plasma from the samples was used for the assay. Leptin levels were measured using a 125I-radioimmunoassay kit (Sensitive Human RIA kit, DRG Germany).

T-test was used to compare nominal variables between the groups. Pearson bivariate correlation analysis was used to evaluate the correlation between breast milk leptin levels and BMI of mothers and weight of infants. All statistical calculations were performed with SPSS. P values below 0.05 were considered as statistically significant.

Results

At the time of leptin assay, body weight of obese infants was significantly higher than that of non-obese infants, but breast milk leptin concentration was not significantly different between mothers of obese and non-obese infants.

There were significant differences in birth weight and length of infants in the two groups (Table 1). In the final analysis, breast milk leptin concentration correlated significantly to the mothers' BMI and weight (Figures 1 and 2).

* *revolutions per minute*

Discussion

Milk leptin concentration of mothers of obese infants did not differ from mothers of non-obese infants.

Serum leptin concentration changes according to weight and adiposity and shows a significant positive correlation with weight and BMI.[12] Bioactive leptin has been detected in infant cord blood.[13-15]

Leptin concentration in cord blood correlated most closely with weight at birth, but also length and head circumference;[16,17] it correlated negatively with infant weight gain.[17] Cord blood leptin produced by the placenta is one of the major sources of leptin in fetal circulation[18] and is thought to play an important role in fetal and neonatal growth.[16-18] Human milk contains many bioactive hormones and peptides which may have roles in neonatal health and development.[18]

In many but not all cases, concentrations of hormones in the milk significantly exceed those found in maternal plasma.[7] Milk-borne hormones may be transported into the milk and modified or synthesized by the mammary glands.[19]

Studies suggest that there is a unique gene and a unique transcript encoding leptin, which is also expressed by the mammary tissue.[20] Leptin in human milk correlates with maternal plasma leptin and reflects maternal adiposity.[21] Obesity is characterized by an excess of adipose tissue relative to the lean body mass. Standard definitions of obesity for infants and children have not been developed. In our study, obesity is defined as age- and gender-specific weight in excess of the 75th percentile on the growth charts of CDC 2000. Total body fat may be measured directly by hydrostatic weighting or by measuring absorption of gases by lipid tissue or level of intracellular potassium; these methods are impractical in the clinical setting.

TABLE 1. Mean and standard deviation of quantitative variables in obese and non-obese infants

Variable	*Obese*	*Non-obese*	*P value (t-test)*
Infant weight (kg)	5.58±0.4	3.150±0.41	0.00
Mother's age (year)	26.82±4.38	27.47±4.85	0.39
Mother's weight (kg)	67.74±11.8	65.28±9.97	0.18
Mother's BMI (kg/m²)	27±4.8	26.35±5.2	0.42
Mother's height (cm)	158.46±5.1	157.93±5.2	0.65
Infant length (cm)	56.74±2.1	54.78±0.41	0.00
Birth weight (kg)	3.5±0.4	3.15±0.41	0.00
Breast milk leptin (ng/dl)	0.44±0.29	0.47±0.39	0.45

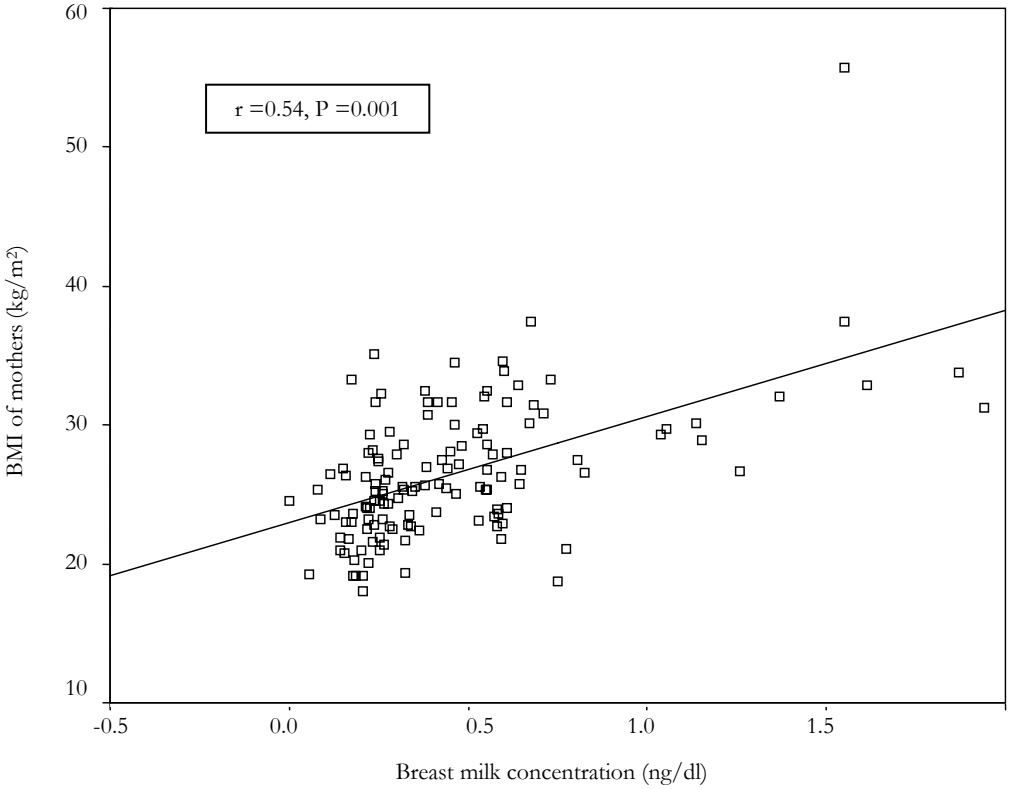

FIGURE 1. Relationship between mothers' BMI and breast milk leptin concentration

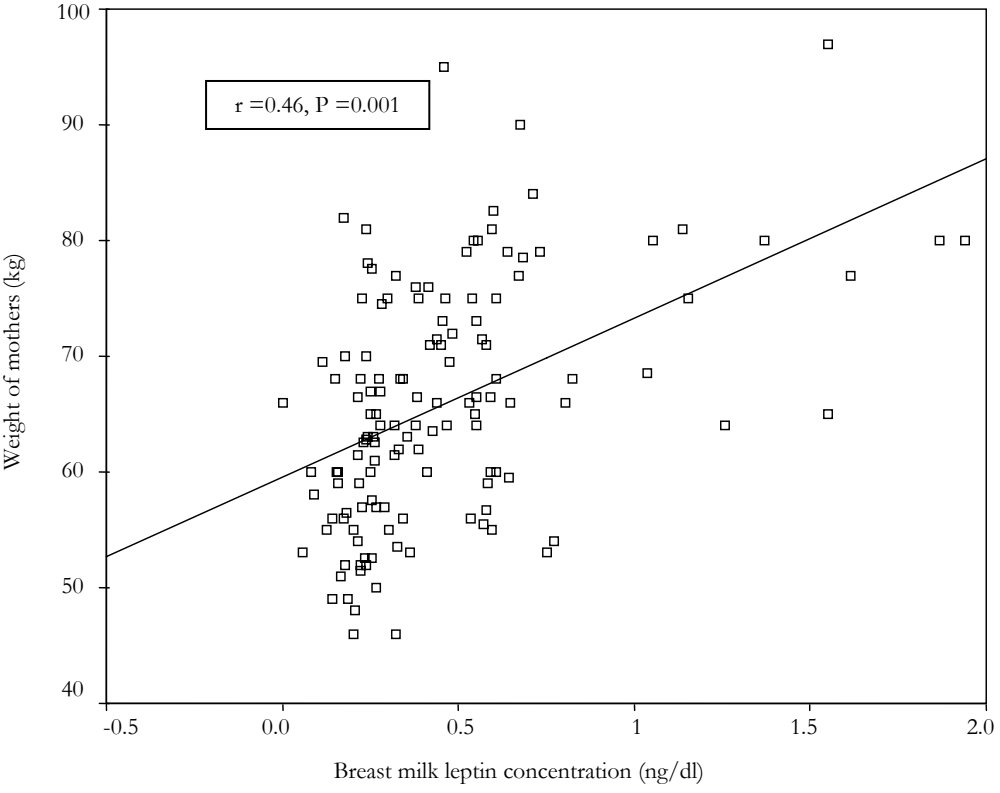

FIGURE 1. Relationship between mothers' weight and breast milk leptin concentration

Thus, indirect methods of assessing obesity, including evaluation of the weight-height ratio and caliper measurement of skin fold thickness are less precise, but less invasive.[22]

Consequently, we used weight-for-age measurement to define obesity in infants in this study, although it was a rough estimation of infant body composition.

In this study, we demonstrated that the leptin concentration of human milk was not different between mothers of obese and non-obese infants.

Moreover, breast milk leptin concentrations correlated with BMI and weight of mothers, but not with weight of infants. These findings suggested that milk-borne leptin has no effect on adiposity during infancy. These results are consistent with the study of Uysal.[23] They reported that milk leptin concentrations were not different in mothers of obese and non-obese infants. Bonnet[34] reported that leptin concentration of milk varies strongly between species and is related to the milk fractions and assay methods used.

If milk leptin levels are found to be significant, this hormone could be involved in neonate physiology. Leptin concentrations of whole milk have been shown to be much higher than those of skim milk and our results were similar to previous studies.[24-26]

Maternal obesity is reportedly associated with increased birth weight; we also found a significant difference between birth weight of infants and weight of mothers at the time of leptin assay. However, Uysal did not find such a relationship; this might have been due to the small number of cases.[23] Human milk contains many hormones and growth factors. It has been proposed that many substances in breast milk may be essential to development of the neonatal small intestine, or have important roles in immune mechanisms.

Leptin has also been reported to have a specific effect on T-lymphocyte responses, differentially regulating the proliferation of memory T-cells, increasing IL-2 production and IFN-γ secretion.[27] Recently, the presence of leptin receptors on gastric mucous cells was demonstrated; it was suggested that leptin might have a paracrine effect.[28]

These observations suggest that leptin in breast milk may have different functions related to the gastrointestinal system or the immune system.

In summary, breast milk leptin concentrations are not different in mothers of obese and non-obese infants. These findings suggest that milk-borne leptin has no significant effect on adiposity during infancy.

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