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# Metabolic Link of Human Milk: Effects on Weight, Length and Body Mass Index (BMI)

**Salah Ahmed Shoheb, Mohamed A.El-Gamasy***

**Abstract**

**Background:** Breast milk adiponectin could play a role in regulation of infants, growth during lactation.

**Aim of work:** To evaluate adiponectin concentration in human milk and to investigate its relationship with serum adiponectin concentration in lactating mothers and their breastfed infants and with anthropometric parameters of infants and mothers.

**Materials and methods:** 60 healthy term infants and their healthy lactating mothers are included at infant age of one month then repeated again at the age of 4 months. All subjects included in this study were subjected to history, clinical examination, investigations including serum level of adiponectin of infants and their mothers by RIA test, Human milk level of adiponectin by ELIZA test.

**Results:** There was a significant decrease in serum adiponectin of infant and mothers and maternal breast milk at age of 4 months (48 ± 6.5,13 ± 1.7, 5.3 ± 2 respectively) when compared to them at the age of 1 month(62.6 ± 1.5, 21.4 ± 5.6, 13.4 ± 3.8 respectively). There was a significant negative correlation between maternal serum adiponectin and BMI of mothers. There was a significant negative correlation between infant serum adiponectin and their weight and length of infants at age of 1 month and at age of 4 months.

**Conclusions:** There's a metabolic link between mothers and their infants through breast milk during 1st 6 months of life. A gradual decline in adiponectin level in maternal breast milk is associated with gradual increase in infant growth up to 6 months of age.

**Keywords:** Human milk; Adiponectin; Anthropometric parameters

## Introduction

Serum adiponectin in infants and mothers as well as in breast milk reach its maximal level during first 6 months of life so exclusive breast feeding should be encouraged. It is recommended to measure infant's serum adiponectin level as well as their mother's serum and breast milk adiponectin especially in infants with retarded growth to exclude hyperadiponectinemia as a possible cause of growth failure.

Human milk contains a wide variety of high biological value proteins that provide adequate nutrition to breast fed infants and simultaneously help in the development of important physiological functions.

Adiponectin, one of the most important hormones related to adipose depots, In addition to its peripheral actions regulating lipids and glucose metabolism [1], adiponectin has central activity in the regulation of energy homeostasis; stimulate food intake and reducing energy expenditure [2].

Adiponectin circulates in human blood as three distinct isomeric forms: Trimeric low molecular weight, hexameric medium molecular weight and high molecular weight (HMW) adiponectin, which consist of large multimers of 12-18 subunits [3]. Recent evidences suggest that HMW adiponectin is the most active form exerting metabolic functions and it is the most abundant form present in HM, suggesting that milk adiponectin could play a significant role in early regulation of infants, growth during lactation [3].

Its plasma concentrations range from 0.5 to 30 µg/ ml, 1000 fold higher than the concentrations of other hormones, such as leptin [2]. A great evidence suggest

**Affiliation:**
*Assistant Professor of Pediatrics, Faculty of Medicine, Tanta University, Egypt*
***Corresponding author:**
Mohamed A.El-Gamasy,
Assistant Professor of Pediatrics,
Faculty of Medicine, Tanta University, Egypt,
Tel: +2 01208136076
E-mail: mgamsy@gmail.com

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that adiponectin serum concentration in neonates and infants is higher than those found in children and adults [4,5]. In previous studies, it has been observed a direct association between cord blood adiponectin concentration and birth weight [4], while other studies have not confirmed this correlation [6].

These finding suggest that prenatal and early post-natal periods are critical for the development of metabolic homeostasis and that adiponectin could play a role in programming of energy balance [7].

The aim of the work is to evaluate adiponectin concentration in human milk and to investigate its relationship with serum adiponectin concentration in lactating mothers and their breastfed infants and with infants, and mothers, anthropometric parameters (weight and length).

## Materials and Methods

### Design of the study and setting

after research ethical committee approval and informed oral or written parental consent from all participants in this research, we performed a cross-sectional study on 60 healthy term infants and their healthy lactating mothers at age of one month then had been studied again at the age of 4 months. All the subjects that enrolled in our study were seen in outpatient clinic of primary health care hospital for brief observation for mild pathological conditions. The study was done in the period between June 2016 and June 2017.

**Inclusion criteria:** Chronological age less than 6 months, Gestational age between 38-42 weeks, Birth weight between 2500-4000 grams, APGAR score higher than 7 at 5 minutes and exclusively breast fed infants.

**Exclusion criteria:** Neonatal diseases, fever, chronic illness, acute disorder compromising growth e.g. acute gastroenteritis or partial breastfeeding. All infants & their lactating mothers included in this study were subjected to the following:

### Full history taking stressing on duration of exclusive breast feeding

**Through clinical examination stressing on Anthropometric evaluation:** Infants were weighted naked before feeding, crown-to-heel length was measured and body mass index (BMI) was calculated by the relation: body weight (Kg) / square of length (m2).We were evaluated anthropometric parameters also in mothers: weight (Kg), height (m) and body mass index (BMI). All anthropometric measurements were taken by a single trained investigator.

**Laboratory investigation**: Serum level of adiponectin for mothers and infants measured by radioimmunoassay test and level of maternal breast milk adiponectin measured by enzyme-linked immunosorbent assay (human adiponectin ELISA kit catalog NoE0605h,Wuhan EIAab Science Co., Ltd, Wuhan, China).

## Statistical Analysis

Data were collected and analyzed using SPSS for windows' (version 12). All Data were expressed in terms of mean ± SD. Comparisons among groups were made using paired t test. 'Two-group comparisons were performed non-parametrically using Mann-Whitney U test'. All statistical tests were two tailed and P<0.05 was considered statistically significant [8].

## Results

Our results showed that 24 (40%) of studied infants were males and 36 (60%) were females with male: female ratio 1: 1.5. Tabel 1 summarized baseline characteristic data of the studied infants and their mothers. This study showed that there is no significant difference in serum adiponectin of infants as regard sex (p>0.05) (Table 1). Table 2 and Figure 2 revealed that there was a significant decrease in serum adiponectin of infant and mothers and maternal breast milk adiponectin at age of 4 months when compared to them at the age of 1 month. Table 2 & 3 and Figures 3 and 4 revealed that there was a significant positive correlation between infant serum adiponection, maternal serum adiponectin and breast milk adiponectin at infant age of 1 month but there was a

**Table 1: Baseline characteristics of studied infants and their mothers**

| | Infants | Mothers |
|---|---|---|
| Age | | |
| Range | 22-38 days | 15-45 years |
| Mean±SD | 30±2.7 days | 30±2.9 years |
| Sex distribution, *n* (%) | | |
| Male | 24 (40) | 0 |
| Female | 36 (60) | 60 (100) |
| Male:female ratio | 1:1.5 | |
| Antenatal history, *n* (%) | | |
| Positive history of diseases associated with or complicating pregnancy | - | 6 (10) |
| Positive history of fetal distress | 4 (6.7) | - |
| Weight (kg) | | |
| 1st month | | |
| Range | 3.25-5.7 | 60-108 |
| Mean±SD | 4.5±0.4 | 84±8.7 |
| 4th month | | |
| Range | 5.5-8 | - |
| Mean±SD | 4.5±0.4 | - |
| Height (cm) | | |
| 1st month | | |
| Range | 50-54 | 154-172 |
| Mean±SD | 52±0.4 | 163±15.4 |
| 4th month | | |
| Range | 56-60 | - |
| Mean±SD | 58±0.6 | - |
| BMI (kg/m²) | | |
| 1st month | | |
| Range | 13-18.7 | 25.3-36.5 |
| Mean±SD | 16.6±0.2 | 31.6±0.3 |
| 4th month | | |
| Range | 17.5–22.2 | - |
| Mean±SD | 20.1±0.2 | - |

**Table 1:** Baseline characteristics od studied infants and their mothers.

| Serum adiponectin of infant | Male (No=36) | Female (No=24) |
|---|---|---|
| Range (µg/ml) | 58 – 73 | 50 – 70 |
| Mean ± SD (µg/ml) | 65.88 ± 511 | 60.50 ± 7.03 |
| T. test | 1.854 | |
| P. value | 0.08 | |

**Table 2:** Comparison between serum adiponectin of infants as regard to sex.

| | | At infant age of 1 monrh | At infant age of 4 months |
|---|---|---|---|
| Serum adiponectin of infant | Range (µg/ml) | 50 – 73 | 40.2 – 60.8 |
| | Mean ± SD(µg/ml) | 62.65 ± 1.51 | 47.99 ± 6.49 |
| | T. test | 7.001 | |
| | P. value | 0.001* | |
| Serum adiponectin of mother | Range (µg/ml) | 12 – 30 | 10 – 16 |
| | Mean ± SD(µg/ml) | 21.36 ± 5.59 | 13.01 ± 1.72 |
| | T. test | 6.378 | |
| | P. value | 0.001* | |
| Adiponectin of breast milk | Range (µg/ml) | 8.07 – 20.0 | 2.90 – 9.20 |
| | Mean ± SD(µg/ml) | 13.38 ± 3.78 | 5.31 ± 2.01 |
| | T. test | 8.448 | |
| | P. value | 0.001* | |

**Table 3:** Comparison between levels of adiponectin of infants' serum, maternal serum and breast milk as regard the age of the studied infants.

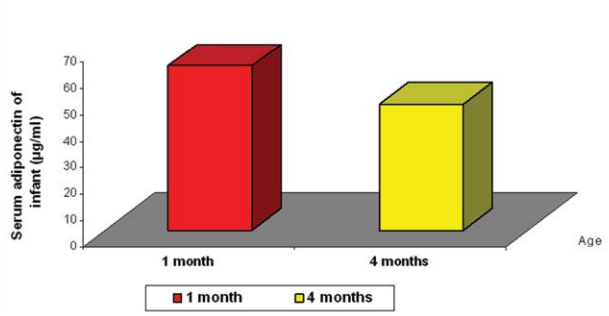


**Figure 1:** Comparison between serum adiponectin of infants as regard age.

| Correlations | | r | p |
|---|---|---|---|
| At age of 1 month | Adiponectin of breast milk (ng/ml) | 0.785 | 0.001* |
| | Serum adiponectin of mother (µg/ml) | 0.774 | 0.001* |
| | Weight of infant (kg) | -0.761 | 0.001* |
| | Length of infant (cm) | -0.788 | 0.001* |
| | Body mass index (BMI )of infant (kg/cm2) | -0.77 | 0.001* |
| At age of 4 months | Weight of infant (kg) | -0.528 | 0.017* |
| | Length of infant | -0.464 | 0.023* |
| | Body mass index (BMI ) of infant (kg/cm$^2$) | -0.607 | 0.005* |

**Table 4:** Correlations between infant serum adiponectin and its level in maternal serum & breast milk and anthropometric measurements of studied infants.

| At age of 1 month | Serum adiponectin of mother (µg/ml) | |
|---|---|---|
| | r | p |
| Adiponectin of breast milk (ng/ml) | 0.784 | 0.001* |
| BMI of mother (kg/m$^2$) | -0.769 | 0.001* |

**Table 5:** Correlations between maternal serum adiponectin, breast milk adiponectin & body mass index (BMI) of mothers at infant age of 1 month.

significant negative correlation between infant serum adiponectin and their anthropometric parameters (weight & length & BMI) of infants at age of 1 month and at age of 4 months.

Table 4 and Figure 5 revealed that there was a significant negative correlation between maternal serum adiponectin and body mass index (BMI) of mothers.

## Discussion

Human milk contains a wide variety of proteins that provide adequate nutrition to breast fed infants and simultaneously help in the development of important physiological functions. Many of These proteins sustain growth; some have role in digestion and utilization of nutrients; some others show antimicrobial action or exert immunomodulatory activities or are growth factors involved in gut maturation of new-borns. All these properties let human milk proteins to contribute to the unique qualities of breast milk [9]. Breastfed infants tend to be healthier than bottle fed infants; they have a lower incidence of allergy and infectious disease and tend to be leaner than formula fed infants [10]. Human milk influences gastrointestinal, neural and immunologic development in breastfeeding infants [10]. Newly identified components of human breast milk especially regulatory metabolic hormones such as adiponectin, leptin, ghrelin and adipocyte fatty acid binding protein [AFABP] are considered to influence nutritional status and possibly play a role in development of components of metabolic syndrome later in adulthood [11]. In our thesis, 20 healthy term infants and their healthy lactating mothers undergoing brief observation for mild pathological conditions in the primary health care unit were observed at age of 1 and 4 months.

As regards to the demographic data, the results showed that 8 out of 20 infants (40%) were males and 12 (60%) were females with male: female ratio 1: 1.5.This study showed that there is no significant difference in serum adiponectin of infants as regard sex ($p>0.05$).These results were in agreement with a study carried by Inami I, et al which revealed that there is no significant difference in serum adiponectin of infants between males and females at age of 1 month [12].

As regard this study, there is a highly significant decrease in serum adiponectin of infants at age of 4 months when compared to it at age of 1 month (62.6 ± 1.5 versus 48 ± 6.5) ($P<0.01$). These results were in agreement with Cesur G, et al who revealed that mean of infant serum adiponectin was 15.09 ± 7.81µg/ml at age of 1 month and was 6.60 ± 7.46 µg/mlat age of 4 months ($P<0.05$) [13]. Our results were also in agreement with Woo JG, et al., who revealed that there is a highly significant decrease in serum adiponectin of infants at age of 12 months (mean= 23.5 ± 0.8 µg/ml ) when compared to it at age of 6 months (mean= 28.6 ± 0.6 µg/ml) and there is a highly significant decrease in serum adiponectin of infants at age of 6 months when compared to it at age of 3 months (mean= 33.2 ± 0.5 µg/ml) but there is significant increase in infant serum adiponectin between base line ( mean=31.1 ± 0.6 µg/ml) and at 3 month ($p<0.01$) [14].

As regard adiponectin in maternal breast milk in our study, there is a highly significant decrease of its levels at infants, age of 4 month when compared to it at age of 1 month (5.3 ± 2 versus 13.4 ± 3.8) ($p<0.001$).These results were in agreement with a study carried by Burner S, et al. who revealed that the median

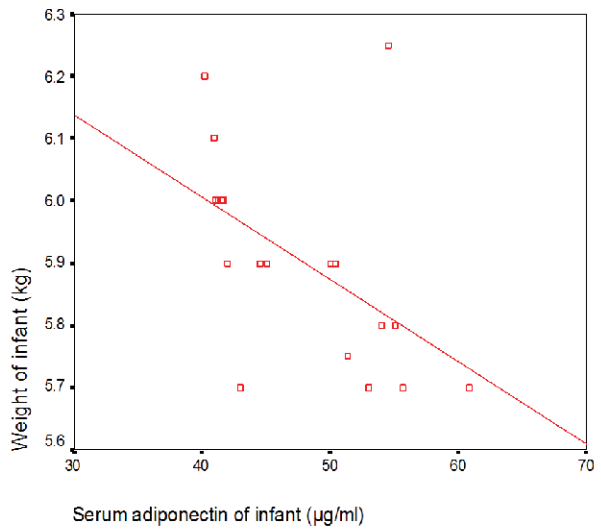


**Figure 2:** Correlation between infant serum adiponectin and weight of infant at age of 1 months.

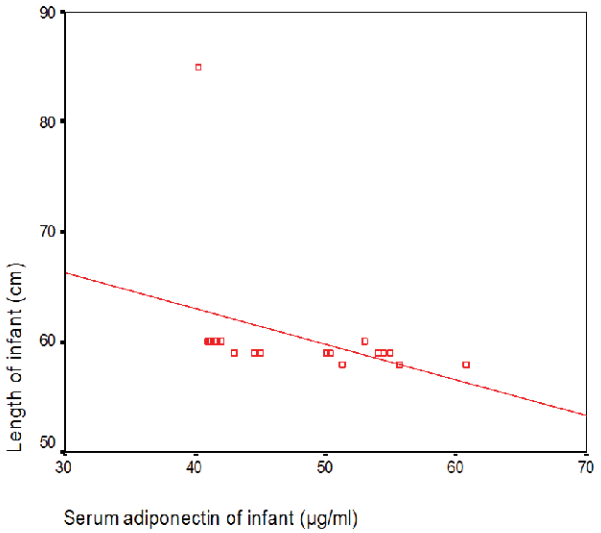


**Figure 3:** Correlation between infant serum adiponectin and length of infant at age of 4 months.

values of both leptin and adiponectin in maternal breast milk were slightly lower at infants, age of 4 month (median= 0.09 ng/ml and 10.36 ng/ml) respectively when compared to them at infants, age of 6weeks (median= 0.11 ng/ml and 10.93ng/ml) respectively (P<0.001) [15]. Another study carried by Bronsky J, et al. revealed that mean value of adiponectin level of breast milk at infant's birth was changeable (22.8 ± 0.8 ng/ml, at age of 1 month, 20.5 ± 0.6 ng/ml was at age of 3 months and 21.4 ± 0.8 ng/ml was at age of 6 months) [16]. Other studies such as a study carried by Cesur G, et al. which revealed no significant difference between maternal breast milk adiponectin at infants, age of 1 month ( mean= 23.61 ± 32.95 ng/ml) and at age of 4 months ( mean= 6.66 ± 9.48 ng/ml) (P > 0.05) [13].

In our study, as regard maternal serum adiponectin, there is a highly significant decrease of maternal serum adiponectinat infants, age of 4 months when compared to it at infants, age of 1month (21.4 ± 5.6 versus 13 ± 1.7 ) (P<0.01). These results were in agreement with Burner S, et al. who revealed that there was a slight decrease in maternal plasma level of high molecular weight adiponectin at infant age of 4 months when compared to it at infant age of 6 weeks with a significant decrease over time [15]. Our results disagreed with a study carried out by Cesur G, et al which revealed that there's no significant difference in maternal serum adiponectin at infants, age of 4 months(mean=7.75 ± 3.67µg/ml) and at infants, age of 1 month (mean=8.36 ± 6.46µg/ml) (P > 0.05) [13]. In our study, there is a significant positive correlation between infant serum adiponectin and their maternal breast milk adiponectinat infants, age of 1 month (r=0.785) (p<0.001). and there is a significant positive correlation between infant serum adiponectin and maternal serum adiponectin at

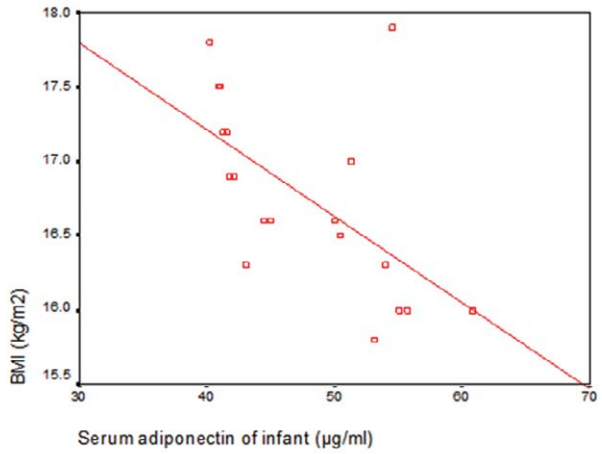


**Figure 4:** Correlation between infant serum adiponectin and body mass index (BMI) of infant at age of 4 months.

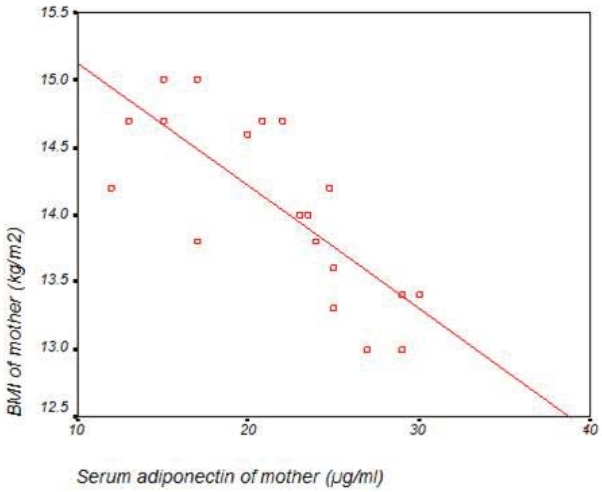


**Figure 5**: Correlation between maternal serum adiponectin & body mass index (BMI) of mothers.

infants, age of 1 month (r = 0.774) respectively (p<0.001). These results were in agreement with Woo JG, et al. who revealed that higher infant serum adiponectin was associated with feeding with breast milk which contains higher level of adiponectin than artificial formula so there is a positive significant correlation between infant and their maternal serum adiponectin (r = 0.29 & p = 0.007) and (r= 0.37 & P= 0.001) at age of birth and 6 months respectively [14]. In our study, there is a significant positive correlation between maternal serum adiponectin and maternal breast milk adiponectin at infants, age of 1 month (r = 0.784) (P = 0.001). These results were in agreement with Woo JG, et al. who revealed that maternal serum adiponectin was significantly correlated with their own median breast milk adiponectin concentration at base line, 3 months and 6 months (r = 0.37 & P<0.001). (14) Also these results were in agreement with Burner S, et al 2014 who revealed that there's a high significant positive correlation between plasma and breast milk levels of adiponectin at infant's age of 6 weeks and 4 months (P<0.001) [15] while these results disagreed with Cesur G, et al who revealed that there was no significant correlation between maternal barest milk and their serum adiponectin (P > 0.05) [13].

This study showed that there is a significant negative correlation between maternal serum adiponectin and their body mass index (BMI at infant's age of 1 month (r = - 0.769 & p = 0.001). These results were in agreement with Matsubara M , et al who revealed that plasma concentration of adiponectin in mothers with highest percentile of BMI (at least 25 kg /m2) were lower than these in the middle (22-25 kg /m2) or lowest (<22kg /m2) percentile of BMI (Mean=6.7 ± 0.3 μg/ml versus 8.6 ± 0.4μg/ml versus 9.2 ± 0.3μg/ml respectively) (P<0.001) [16]. This also in agreement with Nedvidk J, et al. [17] who revealed that adiponectin release in mother's serum is positively correlated with fat size and negatively correlated with BMI. Our results are in agreement also with Hirose H , et al 2010 which revealed that maternal serum high molecular weight (HMW ) adiponectin was negatively correlated with their BMI (mean= 20.6 ± 2.9) (r = - 0.216 & P<0.001) also change in HMW adiponectin level was most strongly correlated with the change in BMI [18].

This study showed that there is a significant negative correlation between infants, serum adiponectin and their anthropometric measurements (weight &length) at infant's age of 1 month and at infants, age of 4 months. These results were disagreed by a study carried out by Cesur G, et al, [13] which revealed that there is a significant positive correlation between level of infant serum adiponectin at age of 1 month and their weight (r = 0.53 & P = 0.020) and also infant serum adiponectin were positively correlated with weight (r = 0.61 &P = 0.006), BMI (r = 0.71 & P = 0.001) at age of 4 months.

## Conclusions

Strengths of this study was it concluded that there was correlations between maternal serum, breast milk adiponectin and infants' serum adiponectin which suggested that there's was a metabolic link between mothers and their infants through breast milk during 1st 6 months of life and that milk adiponectin could play a significant role in early regulation of infants' growth during lactation. Our results suggest that a gradual decline in adiponectin level in maternal breast milk is associated with greater growth (weight gain and fat mass) in their infants up to 6 months of age.

## Recommendations

We recommend encouragements of breast feeding for all infants except for rare contraindications for this beneficial type of feeding. Exclusive breast feeding is essential for 6 months because serum adiponectin in infants and mothers as well as in breast milk reach its maximal level during 6 months of life. Measurement of maternal serum &breast milk adiponectin and infant, serum adiponectin in the first 6 months of life is important for assessing adequate growth of these infants. In infants with retarded growth (weight and / or height), it is recommended to measure their serum adiponectin level as well as their mothers serum and breast milk adiponectin to exclude hyper adiponectinemia as a possible cause of growth failure and that need further research work.

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