Growth Indices of Exclusively Breastfed Until 6 Months Age and Formula-Fed Infants in Southwest of Iran

Abstract

Background: Formula milk is prepared as a nutritional substitution for human breast milk, but because of biologic and constituent differences, it might cause obesity and growth disorders in infants. In this study, we compared the growth pattern of formula-fed and breastfed infants living in Yasuj, southwest of Iran. Methods: Infants 7–14 months of age in southwest of Iran were classified as exclusively breastfed (n = 200) and formula-fed (n = 200) in their first 6 months of life. Growth velocity and Z-scores of weight for age, length for age, weight for length, and head circumference were estimated using WHO Anthro Plus software (2010) and SPSS Version 19 (SPSS Inc., Chicago, IL, USA) using World Health Organization reference for growth data. Results: The study showed that Z-score of length for age and head circumference for age at the birth were significantly lower in formula-fed group than exclusively breastfed group (P < 0.05), but the Z-score of weight for length did not differ significantly. At the sixth month of age, Z-score of weight for length was significantly higher in formula-fed group (P < 0.05), but Z-score of length for age had no significant difference and Z-score of head circumference was higher in exclusively breastfed group yet (P < 0.05). Growth velocity, prevalence of obesity, wasting, underweight, and stunting did not differ between two groups. Conclusions: Our findings suggest that formula feeding can lead to greater weight gain and may help the catch up of length, but evidences are not convincing enough to suggest the formula as an obesogenic feeding in the studied area. To make a conclusion, we suggest comparing the privileged and unprivileged areas and controlling for confounding variables including family hygiene and infant feeding practices between formula-fed and breastfed infants.

Keywords: Breastfeeding, formula feeding, growth velocity

Introduction

Nutrition during infancy could program lifelong risk of obesity and chronic diseases such as hypertension, type 2 diabetes, nonalcoholic fatty liver, and cardiovascular disease.\(^{[1-3]}\) Human breast milk and formula are the main infantile feeding during the first year of life and have important effects on a child’s nutritional status. Some studies reported that breastfeeding is associated with lower adiposity and higher stature in children.\(^{[4,5]}\)

According to the accelerated postnatal weight gain hypothesis, formula feeding increases the fat mass of infants and may be the cause of metabolic disorders in later life;\(^{[1]}\) however, the reports are controversial. While in some studies formula feeding is associated with risk of obesity,\(^{[6,8]}\) others did not report significant difference in body mass index of formula-fed and breastfed infants.\(^{[4,9]}\)

Human breast milk provides all dietary requirements of children until 6 months of age\(^{[10-12]}\) and its composition changes proportionate to the child’s requirements through the infant feeding duration.\(^{[13,14]}\) However, formula milks are significantly different from human milk in the kinetics of a child’s growth.\(^{[15]}\) Growth patterns are evaluated through comparing growth indices at a specific age with a reference chart (prospective assessment) or measuring and comparing the growth indices within a time interval expressed as growth velocity. Growth velocity measurement is a dynamic process, which takes a period of growing child’s life and is a useful index in evaluating nutrition effects and growth monitoring.\(^{[16,17]}\)

Differences in nutritional content and characteristics of human milk and formula milk may affect infant growth.\(^{[18-20]}\) On the other hand, the growth difference between formula-fed and breastfed infants...
may be related to behavioral effects of feeding type or related to developmental situation of society.[13] To compare the effects of formula feeding and breastfeeding on the growth pattern of infants living in Yasuj, we compared anthropometric indices between two groups of exclusively breastfed or formula-fed infants that were matched based on gender and socioeconomic status.

Methods

We conducted this historical cohort study in Yasuj County, southwest of Iran. In all, 400 children 7–14 months of age (200 exclusively breastfed and 200 infant with only formula feeding during the first 6 months of life) referring to health centers were selected. The infants’ gender matched in both groups. The infants’ mothers reported the type of feeding consumed by their children. Inclusion criteria for the breastfed group were exclusively breastfeeding during the first 6 months of life and breast-feeding afterward until weaning. Inclusion criteria for the formula-fed group were formula feeding from the first month of life without breast-feeding. Infants that have fed both breast milk and formula are not included in the comparison. Ethical Committee of Yasuj University of Medical Science approved all the study procedures (ethical code: IR. YUMS. REC.1395.223). Only the children with Iranian ethnicity, born healthy, singleton, and after 37 weeks of gestation, without apparent congenital anomaly, were enrolled in the study. Infants’ demographic information were recorded asking their mothers. Child growth data at birth and 6 months of age were achieved through medical records in healthcare clinics. Weight, length, and head circumference at birth, feeding type until 6 months of age, delivery type, gender, and children birth order were obtained from medical records. Trained health staff measured weight, height, and head circumference for each infant and recorded them in related household file. Weight was measured to the nearest 100 g with the lightest clothing. Length was measured to the nearest 0.5 cm on an infant length board. Z-scores of weight for age, length for age, and head circumference for age were calculated based on World Health Organization reference growth data.[21] Using Anthro software version 3.2.2. Weight-for-age Z-score (WAZ), weight-for-length Z-score (WLZ), and length-for-age Z-score (LAZ) below −2 were identified as underweight, wasting, and stunting, respectively. Weight-for-length Z-score (WLZ) higher than two was regarded as obesity.[17] Weight growth velocity (GV, g/kg/day) was computed for each child. Actual or accurate standard GV (g/kg/day) was calculated using the following formula:[15,22]

$$\text{weight velocity} = \frac{1000(w_i - w_0)}{180(\frac{w_i + w_0}{2})}$$

where $w_o$ = weight in gram at birth and $w_i$ = weight in gram at 6 months of age.

The following procedure was applied to calculate the $Z$-score of weight velocity for an individual child with weight increment $y$ at the visit age $t$ (17):

$$Z_{\text{ind}} = \left[ \frac{Y}{M(t)} \right]^{(t)} - 1 \over S(t)L(t)$$

The above formula was applied to calculate the $Z$-score for velocity of length and head circumference for a child with increment $y$ at the visit age $t$. Detailed explanation and each value of $M(t)$, $L(t)$, $S(t)$, and $\delta$ coefficient for both genders at 6 months of age were provided elsewhere.[21]

Statistical analysis

We analyzed the continuous variables for normality distribution and did not find any serious deviation from normality. Continuous variables were compared using independent samples $t$-test between formula-fed and breastfed groups. Z-score indices in each group were compared at the birth with 6 months of age using paired samples $t$-test. Qualitative variables were compared using Chi-square test. SPSS version 19 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

Tables 1 and 2 summarize the sociodemographic and anthropometric characteristics of infants, respectively. Chi-square test did not show any statistical difference between demographic characteristics of two groups [Table 1].

Birth head circumference in breastfed group was significantly higher than that of formula-fed group ($P < 0.001$). Birth length was also significantly higher in exclusively breastfed group ($P = 0.02$), but the birth weight of both groups was not statistically different.

| Variable                  | Breastfed, $n$ (%) | Formula-fed, $n$ (%) | $P$  |
|---------------------------|-------------------|----------------------|------|
| Infant rank (order)       |                   |                      |      |
| 1                         | 58 (29)           | 64 (32)              | 122 (30.5) | 0.51 |
| 2                         | 76 (38)           | 65 (32.5)            | 141 (35.2) |      |
| ≥3                        | 66 (33)           | 71 (35.5)            | 137 (34.2) |      |
| Mother education (years)  |                   |                      |      |
| 0-5                       | 34 (17)           | 34 (17)              | 68 (17) | 0.94 |
| 6-12                      | 105 (52.5)        | 102 (51)             | 209 (523) |      |
| >12                       | 61 (30.5)         | 64 (32)              | 123 (30.8) |      |
| Father education (years)  |                   |                      |      |
| 1-5                       | 20 (10)           | 13 (6.5)             | 33 (8.2) | 0.56 |
| 6-12                      | 110 (55)          | 98 (48)              | 208 (52) |      |
| >12                       | 70 (35)           | 69 (34.5)            | 159 (39.8) |      |
| Gender                    |                   |                      |      |
| Boy                       | 100 (50)          | 100 (50)             | 200 (50) | 1    |
| Girl                      | 100 (50)          | 100 (50)             | 200 (50) |      |

NS=Not significant
According to Table 3, birth LAZ and birth HCZ in exclusively breastfed group were significantly higher than formula-fed group ($P = 0.005$ and $P = 0.012$, respectively). HCZ of exclusively breastfed group was also significantly higher than formula-fed group at 6 months of age ($P = 0.016$). WLZ of formula-fed group was significantly higher than exclusively breastfed group at the sixth month of age ($P = 0.02$).

Table 4 shows the Z-score changes from birth to sixth month of age in both groups. In the formula-fed group, WAZ, WLZ, and LAZ increased more than breastfed group; however, the increment was just significant for WAZ ($P = 0.021$).

LAZ was significantly lower in boys than girls ($P \leq 0.01$); also, boys had more LAZ at birth and 6 months of age and HCZ at 6 months of age than girls. In addition, the prevalence of obesity, underweight, wasting, and stunting did not differ between exclusively breastfed and formula-fed groups [Figure 1].

**Discussion**

In spite of similar weight for age and WLZ at birth in both groups, we observed that WLZ was significantly higher in formula-fed group at 6 months of age, indicating that formula feeding can lead to a higher weight gain than breast milk in infants. Similar to our findings, Agostoni et al. in an Italian population showed that formula-fed groups had higher weight for length at 12 months of age.$^{[22]}$ In another cohort study, Dewey et al. showed that the mean weight of formula-fed infants was significantly higher than breastfed infants between 6 and 18 months of age.$^{[23]}$ In accordance with our study, other studies also confirmed that formula-fed infants have more weight gain than breastfed infants.$^{[24‑27]}$

These differences may be due to different nutritional contents of human milk and formula milk such as the ratio of omega 3 and omega 6 fatty acids$^{[18]}$ and insulin response to higher amount of protein in formula.$^{[19,20]}$ Furthermore, the growth difference between formula-fed and breastfed infants may also be related to behavioral effects of feeding type or related to developmental situation of society.$^{[13]}$ In spite of higher LAZ in breastfed group at birth, we did not observe the same significant difference among groups at 6 months of age. It means that length for age is compensated in formula-fed group during the first 6 months of life. Comparing the Z-score changes at the sixth month of age showed greater increase in WAZ, LAZ, and WLZ in formula-fed group, but just WAZ was significantly changed. Similar to our study results on LAZ, Bell et al. also reported similar LAZ between formula-fed and breastfed groups.$^{[25]}$ In contrast, in an American study, weight Z-scores of breastfed infants decreased slightly

### Table 2: Anthropometric data of the study population

|                     | Breastfed (n=200) | Formula-fed (n=200) | Total (n=400) | $P$  |
|---------------------|-------------------|---------------------|--------------|------|
| Birth weight (kg)   | 3.2±0.4           | 3.2±0.5             | 3.2±0.5      | 0.19 |
| Birth length (cm)   | 49.5±2.5          | 48.5±2.8            | 49±2.6       | 0.001|
| BHC (cm)            | 34.6±1.2          | 34.3±1.5            | 34.5±1.4     | 0.023|
| Sixth month weight (kg) | 7.9±1             | 7.9±1               | 7.9±1        | 0.9  |
| Sixth month length (cm) | 67.4±2.5         | 66.9±2.8            | 67.1±2.1     | 0.05 |
| Sixth month head circumference (cm) | 43±1.3          | 43±1.4              | 43.2±1.4     | 0.02 |
| Prepregnancy mother weight (kg) | 67±12           | 65.7±10.3           | 66.3±11.2    | 0.25 |
| Pregnancy during weight gain (kg) | 11±3.7          | 11.3±3.8            | 11.1±3.7     | 0.26 |

Continuous variables between formula-fed and exclusive breastfed infants were compared using independent sample t-tests, respectively SD=standard deviation, BHC=birth head circumference

### Table 3: Z-score and velocity of growth indices population of study

|                      | Mother milk fed (n=200) | Formula-fed (n=200) | Total (n=400) | $P$  |
|----------------------|-------------------------|---------------------|--------------|------|
| Birth WAZ            | −0.1±0.9                | −0.3±1.1            | −0.3±1       | 0.06 |
| Birth WLZ            | −0.25±1.3               | 0.01±1.4            | −0.2±1.4     | 0.13 |
| Birth LAZ            | 0.07±1.1                | −0.25±1.2           | 0.1±1.1      | 0.005|
| Birth HCZ            | 0.38±0.94               | 0.11±1.2            | 0.24±1.1     | 0.012|
| Sixth month WAZ      | 0.25±1.3                | 0.31±1.1            | 0.27±1.2     | 0.26 |
| Sixth month WLZ      | 0.12±1.26               | 0.41±1.21           | 0.27±1.2     | 0.020|
| Sixth month LAZ      | 0.3±1                   | 0.25±1.3            | 0.28±1.1     | 0.56 |
| Sixth month HCZ      | 0.5±1                   | 0.3±1.2             | 0.4±1.1      | 0.016|
| Weight velocity      | 0.4±1.2                 | 0.5±1.1             | 0.45±1.1     | 0.35 |
| Height velocity      | 1.7±0.3                 | 1.8±0.3             | 1.75±0.3     | 0.91 |
| Head circumference Z-score | 0.03±1             | 0.1±1               | 0.06±1       | 0.49 |
| Velocity Z-score     | 4.7±0.6                 | 4.8±0.7             | 4.76±0.3     | 0.21 |

WAZ=weight-for-age Z-score, NS=not significant, LAZ=length-for-age Z-score, HCZ=head circumference-for-age Z-score, WLZ=weight-for-length Z-score


In this study, HCZ was significantly higher in breastfed than formula-fed group at birth and at 6 months of age. However, the change in HCZ is the same in both the groups and the observed difference could be due to baseline difference in HCZ in the two groups. Brain tissue is a rapidly synthesizing tissue during the last pregnancy trimester and neonatal period. Infant mental development and brain growth need docosahexaenoic acid (DHA) and arachidonic acid (AA). Because of incomplete enzymatic activity, the synthesis of AA and DHA from their precursor fatty acid is negligible in fetus and infants. Therefore, the AA and DHA requirements must be provided from the mothers’ diet during prenatal period or breastfeeding postnatal. From the sixth week of lactation to the sixth month, the fat and polyunsaturated fatty acid content of human milk increases, thus breastfeeding in this period is significant to child’s nutrition.

Researchers propose that because of late assessment the consequences of human milk fatty acids on brain development are unknown. Although breast milk has lower protein than formula milks, overall amino acid profile of human milk fulfills needs of developing infant systems. For instance, glutamine, the most abundant free amino acid in human milk, might play a neurotransmitter role in the brain. Most of the formula milks are manufactured from milk of mammalians such as cow; however, these milk fats cannot substitute human milk. Even human breast milk in mothers delivering preterm babies contains higher DHA and AA than milk from mothers delivering full-term babies. In this study, growth velocity indices did not significantly differ based on feeding type at first 6 months of age; it may be because of research design in our study or the small sample size. These indices are used in longitudinal studies for assessing the growth patterns.

## Conclusions

Our findings show that formula feeding may increase body weight more than human breast milk. In addition, it may compensate for the length growth retardation that is frequently seen in unprivileged children. In addition, it may make formula-fed infants prone to overweight and obesity in privileged children. However, because of small sample size and cross-sectional design of our study, we must interpret these findings with caution. For a conclusion, we suggest implementing the study as cohort group comparing privileged and unprivileged areas and controlling for infants hygiene and other feeding practices.

## Financial support and sponsorship

This study is financially supported by Deputy of Research and Technology of the Yasuj University of Medical Sciences.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Ziegler EE. Growth of breast-fed and formula-fed infants. Nestle Nutr Workshop Ser Pediatr Program 2006;58:51-9.
2. Johnson L, Llewellyn CH, van Jaarsveld CH, Cole TJ, Wardle J. Genetic and environmental influences on infant growth: Prospective analysis of the Gemini twin birth cohort. PLoS One 2011;6:e19918.
3. Rzehak P, Oddy WH, Mearin ML, Grote V, Mori TA, Szajewska H, et al. Infant feeding and growth trajectory patterns in childhood and body composition in young adulthood. Am J Clin Nutr 2016;106:568-80.
4. Martin RM, Patel R, Kramer MS, Guthrie L, Vilchuck K, Bogdanovich N, et al. Effects of promoting longer-term and exclusive breastfeeding on adiposity and insulin-like growth factor-I at age 11.5 years: A randomized trial. JAMA 2013;309:1005-13.
5. Hosseini SM, Maracy MR, Sarrafzade S, Kelishadi R. Child weight growth trajectory and its determinants in a sample of Iranian children from birth until 2 years of age. Int J Prev Med 2014;5:348-55.
6. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Effect of infant feeding on the risk of obesity across the life course: A quantitative review of published evidence. Pediatrics 2005;115:1367-77.
7. Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: A meta-analysis. Am J Epidemiol 2005;162:397-403.
8. Arenz S, Rückerl R, Koletzko B, von Kries R. Breast-feeding and childhood obesity – A systematic review. Int J Obes Relat Metab Disord 2004;28:1247-56.
9. Owen CG, Martin RM, Whincup PH, Davey-Smith G, Gillman MW, Cook DG. The effect of breastfeeding on mean body mass index throughout life: A quantitative review of...
published and unpublished observational evidence. Am J Clin Nutr 2005;82:1298‑307.
10. Lessen R, Kavanagh K. Position of the academy of nutrition and dietetics: Promoting and supporting breastfeeding. J Acad Nutr Diet 2015;115:444‑9.
11. Martin CR, Ling PR, Blackburn GL. Review of infant feeding: Key features of breast milk and infant formula. Nutrients 2016;8: pii: E279.
12. Ballard O, Morrow AL. Human milk composition: Nutrients and bioactive factors. Pediatr Clin North Am 2013;60:49‑74.
13. ESPGHAN Committee on Nutrition, Agostoni C, Braegger C, Decsi T, Kolacek S, Koletzko B, et al. Breast‑feeding: A commentary by the ESPGHAN committee on nutrition. J Pediatr Gastroenterol Nutr 2009;49:112‑25.
14. Disantis KI, Collins BN, Fisher JO, Davey A. Do infants fed directly from the breast have improved appetite regulation and slower growth during early childhood compared with infants fed from a bottle? Int J Behav Nutr Phys Act 2011;8:89.
15. Ayatollahi SM, Haem E, Sharafi Z. Growth velocity of infants from birth to 5 years born in Maku, Iran. Glob J Health Sci 2015;8:56‑63.
16. Ghaemmaghami P, Ayatollahi SM, Alinejad V, Haem E. Longitudinal standards for growth velocity of infants from birth to 4 years born in west Azerbaijan province of Northwest Iran. Epidemiol Health 2015;37:e2015029.
17. Ailhaud G, Guesnet P. Fatty acid composition of fats is an early determinant of childhood obesity: A short review and an opinion. Obes Rev 2004;5:21‑6.
18. Bergeron K, Julien P, Davis TA, Myre A, Thivierge MC. Long‑chain n‑3 fatty acids enhance neonatal insulin‑regulated protein metabolism in piglets by differentially altering muscle lipid composition. J Lipid Res 2007;48:2396‑410.
19. Singhal A, Lucas A. Early origins of cardiovascular disease: Is there a unifying hypothesis? Lancet 2004;363:1642‑5.
20. WHO Multicentre Growth Reference Study Group, WHO Child Growth Standards: Growth velocity based on weight, length and head circumference: Methods and development. Geneva: World Health Organization, 2009. p. 242.
21. Patel AL, Engstrom JL, Meier PP, Jegier BJ, Kimura RE. Calculating postnatal growth velocity in very low birth weight (VLBW) premature infants. J Perinatol 2009;29:618‑22.
22. Agostoni C, Grandi F, Gianni ML, Silano M, Torcoletti M, Giovannini M, et al. Growth patterns of breast fed and formula fed infants in the first 12 months of life: An Italian study. Arch Dis Child 1999;81:395‑9.
23. Dewey KG, Heinig MJ, Nommsen LA, Peerson JM, Lönnerdal B. Growth of breast‑fed and formula‑fed infants from 0 to 18 months: The DARLING study. Pediatrics 1992;89:1035‑41.
24. Kramer MS, Guo T, Platt RW, Sevkovskaya Z, Dzikovich I, Collet JP, et al. Infant growth and health outcomes associated with 3 compared with 6 mo of exclusive breastfeeding. Am J Clin Nutr 2003;78:291‑5.
25. Bell KA, Wagner CL, Feldman HA, Shypailo RJ, Belfort MB. Associations of infant feeding with trajectories of body composition and growth. Am J Clin Nutr 2017;106:491‑8.
26. de Bruin NC, Degenhart HJ, Gål S, Westerterp KR, Stijnen T, Visser HK, et al. Energy utilization and growth in breast‑fed and formula‑fed infants measured prospectively during the first year of life. Am J Clin Nutr 1998;67:885‑96.
27. Butte NF, Wong WW, Hopkinson JM, Smith EO, Ellis KJ. Infant feeding mode affects early growth and body composition. Pediatrics 2000;106:1355‑66.
28. Joardar A, Sen AK, Das S. Docosahexaenoic acid facilitates cell maturation and beta‑adrenergic transmission in astrocytes. J Lipid Res 2006;47:571‑81.
29. Lönnerdal B. Biological effects of novel bovine milk fractions. Nestle Nutr Workshop Ser Pediatr Program 2011;67:41‑54.
30. van de Lagmaat M, Rotteveel J, Muskiet FA, Schaafsma A, Lafeber HN. Post term dietary‑induced changes in DHA and AA status relate to gains in weight, length, and head circumference in preterm infants. Prostaglandins Leukot Essent Fatty Acids 2011;85:311‑6.