Appropriate infant feeding practices result in better growth of infants and young children in rural Bangladesh

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ABSTRACT


Objective: We evaluated the effects of following current infant feeding recommendations on the growth of infants and young children in rural Bangladesh.

Design: The prospective cohort study involved 1343 infants with monthly measurements on infant feeding practices (IFPs) and anthropometry at 17 occasions from birth to 24 mo of age to assess the main outcomes of weight, length, anthropometric indexes, and undernutrition. We created infant feeding scales relative to the infant feeding recommendations and modeled growth trajectories with the use of multilevel models for change.

Results: Mean (±SD) birth weight was 2697 ± 401 g; 30% weighed < 2500 g. Mean body weight at 12 and 24 mo was 7.9 ± 1.1 kg and 9.7 ± 1.3 kg, respectively. More appropriate IFPs were associated (P < 0.001) with greater gain in weight and length during infancy. Prior IFPs were also positively associated (P < 0.005) with subsequent growth in weight during infancy. Children who were in the 75th percentile of the infant feeding scales had greater (P < 0.05) attained weight and weight-for-age z scores and lower proportions of underweight compared with children who were in the 25th percentile of these scales.

Conclusions: Our results provide strong evidence for the positive effects of following the current infant feeding recommendations on growth of infants and young children. Intervention programs should strive to improve conditions for enhancing current infant feeding recommendations, particularly in low-income countries. Am J Clin Nutr 2008;87:1852–9.

INTRODUCTION

Proper feeding practices during infancy are essential for attaining and maintaining proper nutrition, health, and development of infants and children (1–4). Results of studies on infant and child feeding have indicated that inappropriate feeding practices can have profound consequences for the growth, development, and survival of infants and children, particularly in developing countries (4–11).

The World Health Organization (WHO) recommends exclusive breastfeeding for the first 6 mo of life and continuation of breastfeeding for 2 y (12). The WHO and the United Nations International Children’s Emergency Fund (UNICEF) have articulated a global strategy for infant and young child feeding (13) and recommendations in the form of guiding principles for complementary feeding of the breastfed child (14) to focus attention on the effect of feeding practices on health and growth of infants and young children. Although these feeding recommendations were based on the evidence available in the published literature, the effects of following these recommended infant feeding practices (IFPs) on growth during infancy and early childhood have not been evaluated.

Most studies on the association between feeding practices and growth during infancy and childhood primarily investigated the growth and other health outcomes of infants and children in relation to breastfeeding (15–19) and the timing and type of introduction of complementary foods (5, 16, 20, 21). Most studies on the association between feeding practices during infancy and childhood and growth of infants and children were based on cross-sectional data (22–24). The associations that were observed in the cross-sectional studies do not preclude the possibility of reverse causality (25, 26). In several longitudinal studies, the associations between IFPs and the growth of infants and children were observed (5, 16, 20, 21). These studies, however,
did not evaluate the effect of current infant feeding recommendations by the WHO and UNICEF.

In this study, we evaluated the effects of following the recommended IFPs on the growth of infants and young children in rural Bangladesh. We proposed that the infants who were fed following the current infant feeding recommendations would grow better during infancy and early childhood. We used an innovative approach to construct the infant feeding scales that were cumulative and captured the feeding practices of all prior periods. We followed appropriate analytic techniques to investigate the longitudinal association between IFPs and growth of infants and young children with the use of multilevel models for change. This analytic approach prevented the potential problem of reverse causality that can be present in cross-sectional studies.

SUBJECTS AND METHODS

Study population and data source

We used data from the Maternal and Infant Nutrition Intervention in Matlab (MINIMat) trial. The prospective cohort was a subset of infants born to women participating in the MINIMat trial that included a follow-up of infants from birth to 2 y. The study was conducted in Matlab, Bangladesh.

The enrollment of pregnant women in the MINIMat trial took place between November 2001 and October 2003. We selected all children (n = 1343) who were born between May 2002 and December 2003 and had completed 24 mo of follow-up in December 2005. The mothers of these children received a food supplement starting at ≈17 wk of gestation and received health education messages either with or without randomly assigned intensive breastfeeding counseling during pregnancy and after delivery. Data on IFPs and morbidity were collected monthly during the first year and quarterly during the second year of life. The mothers of these children were followed during pregnancy when data on socioeconomic status (SES) and maternal weights were collected.

Data collection and quality control of data

All data were collected at the women’s homes by trained interviewers and paramedics. Structured questionnaires with precoded and open-ended questions were used for data collection. All questionnaires were pretested and revised accordingly. The questionnaires were first prepared in English and then translated into Bangla. Informed consent was obtained from the women about their participation in the study. The study was approved by the Research Review Committee and Ethical Review Committee of the International Centre for Diarrhoeal Disease Research, Bangladesh, and the University Committee on Human Subjects at Cornell University.

Infant feeding practices

We created infant feeding scales using data collected monthly until 12 mo of age. Mothers were asked to recall about general feeding patterns in the previous month, ie, whether the baby was still breastfed, and the feeding of plain water: water containing sugar, glucose, or jaggery (ie, unrefined brown sugar made from the sap of the date palm or sugarcane); fruit juice; cow milk; and semisolid and solid foods. The data also included the first food given to the baby, timing of breastfeeding initiation, anything given to the baby before giving breast milk, colostrum rejection, number of times the baby was breastfed during the day and night, and the use of a bottle with a nipple to feed the baby.

The response for most items was “yes” or “no.” We scored each item depending on whether a practice was appropriate based on the current infant feeding recommendations of the WHO and UNICEF (13, 14). For example, a practice that was appropriate for a specific age group received a score of 1, and a practice that was inappropriate received a score of 0. Practices that are considered particularly appropriate for a given age received a score of 2. For example, breastfeeding received a score of 2 for infants from birth to 12 mo of age. A score of 0 was given to nonbreastfed infants. Use of a baby bottle with a nipple was scored as 0 because the practice is considered inappropriate for all age groups; avoidance of baby bottles received a score of 1, indicating an appropriate practice.

We included only infants who were not given any food other than breast milk during the first month to be considered as exclusively breastfed at 1 mo of age. We included only those infants who were exclusively breastfed at 1 mo and were not given any food other than breast milk during the second month to be considered as exclusively breastfed at 2 mo of age and so on. We used information on whether a food was given in the first or second half of the month. Thus, the estimate of the duration of exclusive breastfeeding was close to reality because of the longitudinal nature of infant feeding data, but we could not avoid potential errors of 2 wk in estimating the duration of exclusive breastfeeding because we lacked information on the exact date of giving any food.

We created cumulative infant feeding scales that were specific for different age groups (eg, 3, 6, 9, and 12 mo) because different practices are required for each age group. First, we created a feeding scale for each month from 1 to 12 mo. Then we computed cumulative feeding scales for different age groups by adding all the monthly feeding scales of those particular age groups with the feeding scales of the preceding months. For example, we computed cumulative feeding scale at 3 mo by adding the individual feeding scales from 1 to 3 mo (feeding scale at 3 mo = feeding scale at month 1 + . . . + feeding scale at month 3). We followed the same strategy to create cumulative feeding scales at 6, 9, and 12 mo.

We examined whether the infants who were missing data on early feeding practices differed from those who were not missing these data. We compared these 2 groups on their birth weight, household food security, and other key baseline SES variables. For the continuous variables, we used a t test for equality of means, and, for the categorical variables, we used Pearson’s chi-square tests. These 2 groups of infants did not differ, based on these baseline variables.

We standardized the feeding scales by converting the original scores into percentages of the maximum total scores of the theoretical scales. Descriptive statistics of the infant feeding scales are provided in Table 1. A higher score in the feeding scales indicated a better IFP. These scales were used as continuous variables in the analyses. The reliability (ie, Cronbach’s α) of these feeding scales was 0.6–0.8.

Morbidity

We created morbidity scales based on the presence or absence of the illnesses during the preceding 7 d, signs and symptoms of the illnesses and their severity, and health care seeking. The
variables that were included in the morbidity scales were fever, cough or difficult breathing, diarrhea, any other illness, and treatment received in the past 1 mo. Absence of any of these illnesses received a score of 1 and their presence received a score of 2. We used available information that was collected along with diarrhea (eg, blood in the stool, associated vomiting, etc) and cough (difficult breathing and rapid breathing or chest indrawing) to indicate the severity of diarrhea and respiratory symptoms. We also included information on whether any health care was sought for the infant in the past month, which also may reflect the severity of the illness.

We created a monthly morbidity scale of 1 through 12 mo by adding the scores assigned on 12 items of the morbidity scale. We used the mean of the morbidity scales of the preceding periods for the morbidity scale of that particular age group. For example, we used the mean of morbidity scales at 1, 2, and 3 mo for the morbidity scale at 3 mo. We followed the same strategy for morbidity scales at 6, 9, and 12 mo. Descriptive statistics of the morbidity scales are provided in Table 1. A higher score in the scale indicated a more severe illness. The reliability of each morbidity scale was 0.7.

### Wealth index

We used a wealth index as a measure of SES that was created by the MINIMat team from the information on household assets. The included variables were land (homestead, land under cultivation, fallow land, pond or ditch, and family land), construction materials of the walls of the house, ownership of household assets (clock or watch, chair or table, almirah, bicycle, radio, television, electric fan, cows, goats, and chicken or ducks), sarees (a traditional garment worn by women in Bangladesh or from the Indian subcontinent) or shalwar-kameez (a pair of loose-fitting pleated trousers tapering to the ankle, worn by women, usually under a long tunic) owned for ceremonial use, and pairs of shoes or sandals owned.

Total land was computed by adding homestead land, land under cultivation, and fallow land. Total land was categorized into groups of 0, >0–5, >5–25, >25–90, and >90 decimals (approximately equal to 1/100 acre). The categories for pond or ditch and family land were either yes or no. The categories for construction materials of the walls of the house were brick or cement, tin, bamboo, and other. For household assets, categories for each item were owned or not owned by the household. Total number of clothes was obtained by adding sarees and shalwar-kameez, which was categorized into 0–3, 4–9, 10–17, and >18. The categories for shoes or sandals were 0, 1, 2, and >2.

Principal component analysis was used to create the wealth index. A weight was attached to each item from the first principal component. Households were divided into SES quintiles based on wealth index: quintile 1 (poor), quintile 2 (lower middle), quintile 3 (middle), quintile 4 (upper middle), and quintile 5 (rich).

### Anthropometry

All birth weights were measured by electronic or beam scales, which were precise to 10 g (UNICEF Uniscale; SECA Gmbh & Co, Hamburg, Germany). Locally manufactured, collapsible length boards, which were precise to 1 mm, were used to measure recumbent lengths of the baby, including birth length. Maternal weights were measured by electronic scales (Uniscale; SECA), which were precise to 100 g. Interviewers who collected birth measurements and infant follow-up data were specially trained on anthropometric measurements. All measuring scales were standardized daily. Weight and length measurements were converted to weight-for-age \( z \) (WAZ), length-for-age \( z \) (LAZ), and weight-for-length \( z \) scores according to the WHO Multicenter Growth Reference Study child growth standards (27). We used ANTHRO 2005 from the WHO website (http://www.who.int/childgrowth/) for this conversion. We also calculated body mass index (BMI; in kg/m\(^2\)) and BMI-for-age \( z \) scores according to the new WHO standards.

A cutoff of \(-2\) \( z \) score for these indexes was used for classifying children as undernourished (\( z \leq -2 \)) or well-nourished (\( z > -2 \)). Underweight and stunting were defined as \( z \leq -2 \) and \( z \leq -2 \) respectively. Wasting was defined as \( z \leq -2 \) or weight-for-length or BMI-for-age \( z \) score.

### Statistical analysis

We used multilevel models for change to model weight and length trajectories of the infants and young children (28, 29). These models were appropriate for longitudinal data with repeated-measures in which several individual measurements (follow-up measurements on weight and length) are nested within persons (infants and children). The models included components at 2 levels: 1) a level-1 submodel that described how individual children changed over time (within-child), and 2) a
RESULTS

General and baseline characteristics

Mean (±SD) birth weight and birth length of the newborns were 2697 ± 401 g and 47.8 ± 2.1 cm, respectively. Overall, 30% of the babies were born with low birth weight (<2500 g). The boys differed from the girls in mean birth weight (2741 ± 411 g compared with 2650 ± 384 g; \( P < 0.001 \)), mean birth length (48.0 ± 2.1 cm compared with 47.5 ± 2.1 cm; \( P < 0.001 \)), and the rate of low birth weight (26.0% compared with 34.5%). Attained body weight at 6, 12, and 24 mo was 6.71 ± 0.91 kg, 7.93 ± 1.10 kg, and 9.72 ± 1.29 kg, respectively. Mean weight deficits relative to the new WHO standards were 0.91 kg, 1.37 kg, and 2.10 kg at 6, 12, and 24 mo, respectively. Mean age of the mothers was 26.3 ± 5.8 y, and they were light (46.5 ± 6.6 kg) with low parity (median: 1; range: 0–7). The mean education (completed years) of these women and their husbands was 5.0 ± 4.1 y and 5.4 ± 4.5 y, respectively.

Infant feeding patterns

Colostrum and prelacteal feeding

About 92% of mothers gave colostrum to their infants, and only 8% of them gave prelacteal food or drink (3.2% of mothers gave honey; 1.3% mustard oil; 2.8% sugar, glucose, or jaggery water; and ~1% of them gave either plain water or other milk before giving breast milk).

Breastfeeding: types and duration

Almost all infants in this sample (99.4%) were breastfed at 1 mo of age and 92% of them were still breastfeeding at 12 mo of age (Figure 1). The proportion of infants who were exclusively breastfed decreased from 78.3% at 1 mo of age to 10.7% at 6 mo of age. The median duration of exclusive breastfeeding was \( \approx 121 \) d. The median duration of any breastfeeding was \( \approx 365 \) d in the first year of life.

Liquids: plain water, fruit juice, other liquids, and cow milk

About 3.7% of infants were given plain water even at 1 mo of age that increased to 76.0% and 97.2% at 6 and 9 mo of age, respectively (Figure 1). The proportions of infants given fruit juice were low during the first 5 mo of age and increased to 37.3% at 6 mo of age. The feeding of other liquids (such as sugar, glucose, or jaggery water) was generally low and increased with the age of infants. Some infants were fed cow milk, starting at 1 mo of age that reached 41.0% at 6 mo of age.

Semisolid and solid foods

Only 2.2% of infants were given semisolid foods at 1 mo of age (Figure 1). This proportion increased as the infants got older. At

![Figure 1. Infant feeding practices by age of infants and the proportion of infants who were exclusively breastfed and given various types of food in addition to breast milk (BM). Infants whose intake was classified as BM and consuming plain water only consumed no supplements. The intake of infants who received BM and water-based liquids (fruit juice and other liquids (sugar, glucose, or jaggery water)) and who did not receive complementary foods was classified as BM and nonmilk liquids; even they might also get plain water. Jaggery is sugar or unrefined brown sugar made from the sap of the date palm. Infants whose intake was classified as BM and cow milk were fed BM and cow milk as well as plain water and any other liquids. Infants who got complementary food (semisolids and solids) were classified as BM and complementary foods as long as they also were breastfed.](https://example.com/figure1.png)
6 mo of age, about half (49.6%) of the infants were given semi-solid foods and about two-thirds (66.4%) at 9 mo of age. The proportion of infants who was given solid foods was low until 5 mo of age (13.2%) but increased rapidly thereafter (43.9% at 6 mo of age and 94.1% at 10 mo of age). Overall, 2.4% of infants were given complementary foods at 1 mo of age. At 6 mo of age, two-thirds (66.7%) of infants were fed with complementary foods that increased to 95% at 9 mo of age.

**IFPs and growth in weight and length during 1–12 mo**

As expected, more appropriate IFPs were significantly \( P < 0.001 \) associated with gain in weight and length during 1–12 mo of age (Table 2, model 1). The association between IFPs during infancy and gain in weight and length from 1 to 12 mo of age remained in the adjusted models with other infant (Table 2, model 2) and maternal (Table 2, model 3) variables. We found similar associations when WAZ and LAZ scores were used as dependent variables (data not shown).

**Prior IFPs and subsequent growth in weight and length**

IFPs at 1–3 mo of age were significantly associated \( P < 0.001 \) with gain in weight from 3 to 12 mo of age in the fully adjusted model with other infant and maternal variables (Table 3). Similarly, IFPs at 1–6 mo of age were associated \( P < 0.005 \) with gain in weight from 6 to 12 mo of age. IFPs at 1–9 mo of age, however, were not associated with gain in weight during 9–12 mo of life. Similarly, IFPs during 1–12 mo were not significantly associated with gain in weight in the second year of life. Prior IFPs were not significantly associated with the subsequent gain in length during infancy and in the second year of life (data not shown).

**Attained weights and WAZ scores of children**

The attained weights of the children who were in the 75th percentile of infant feeding scales of 1–3, 1–6, 1–9, and 1–12 mo were greater \( P < 0.05 \) than those of the children in the 25th percentile of these scales during the subsequent periods until 24 mo of age (data not shown). The WAZ scores of the children in the 75th percentile were greater than those of the children in the 25th percentile of the infant feeding scales of 1–6 mo (Figure 2A) and 1–12 mo (Figure 2B). We observed similar results for the infant feeding scales of 1–3 and 1–9 mo.

**TABLE 2**

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<thead>
<tr>
<th>IFP</th>
<th>Weight</th>
<th>Length</th>
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<tr>
<td></td>
<td>( \beta (SE) )</td>
<td>( P )</td>
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<tr>
<td>Model 1(^1)</td>
<td>3.0 (0.0)</td>
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<tr>
<td>Model 2(^2)</td>
<td>3.0 (0.0)</td>
<td>0.001</td>
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<tr>
<td>Model 3(^3)</td>
<td>3.0 (0.0)</td>
<td>0.001</td>
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\(^1\) One-month lagged IFPs were used for the corresponding weight.

\(^2\) SE of regression coefficients in parentheses.

\(^3\) Only IFP in the model.

\(^4\) Model 1 with additional control for other infant variables: sex, morbidity, birth weight, and birth length.

\(^5\) Model 2 with additional control for maternal variables: age, weight, education, and wealth index.

**IFP and nutritional status**

As expected, higher proportions of children in the 25th percentile of the infant feeding scales were underweight than their counterparts in the 75th percentile of the infant feeding scales of...
1–6 mo (Figure 3A) and 1–12 mo (Figure 3B). These differences were statistically significant ($P < 0.05$) at 12 and 24 mo of age. We found similar patterns for the infant feeding scales of 1–3 and 1–9 mo.

**DISCUSSION**

We evaluated the effect of IFPs relative to the current infant feeding recommendations on growth of infants and young children in a low-income country. Use of longitudinal data and appropriate analytic techniques permitted us to establish the highly plausible temporal relation between IFPs and growth during infancy and early childhood. Our results suggest that following the recommended IFPs had positive effects on gain in weight and length during infancy. These findings underscore the importance of following the current infant feeding recommendations to ensure better growth during infancy, particularly in developing countries such as Bangladesh.

**Infant feeding practices and growth**

As expected, following the recommended IFPs was positively associated with gains in weight and length of this sample during infancy. Comparisons of the attained weights of the children in the 25th and 75th percentiles of infant feeding scales also indicated the relative importance of following recommended IFPs for growth of infants. As expected, the attained weight was greater for those who were in the 75th percentile than for those who were in the 25th percentile of the feeding scales. Because the infant feeding scale of 1–12 mo captured the feeding practices from 1 to 12 mo of age, its effect on the attained weights was more obvious during the second year of life. IFPs of 1–12 mo, however, were not significantly associated with gain in weight in the second year of life in the multilevel model analysis. Although the observed weights of the children in the 75th percentile were greater than those of the children in 25th percentile, the rates of growth of the children in the 25th and 75th percentiles were not significantly different during the second year life.

The first year of an infant’s life is the period of most rapid growth and an important nutrition transition, when infants are given various types of complementary foods along with breast milk. Our results suggest that recommended IFPs of the prior periods were important for the gain in weight of the subsequent periods during infancy. In particular, feeding practices during the first quarter and the first half of infancy were significant for the subsequent gain in weight during infancy. A 10% increase in the feeding scale of 1–3 mo and 1–6 mo would increase gain in weight by 90 g and 70 g, respectively. Because weight is more sensitive than length to short-term dietary changes (30) and also to childhood illnesses (31–35), our results of the positive association between IFPs and weight growth during infancy corroborates the importance of following infant feeding recommendations.

Although the associations between IFPs and gain in length during 1–12 mo of life were statistically significant, they were not biologically important. A 10% increase in the feeding scale would cause only a 0.05-cm gain in length during infancy. The small effect of following the infant feeding recommendations on length may result because these infant feeding scales were relatively crude. They did not capture the multidimensional nature of IFPs that might contribute to better linear growth. Our results showed that the mothers fed their infants energy-rich liquids, such as fruit juice and sugar, glucose, or jaggery water even during the earlier months of life, but we do not have information whether they fed their infants foods that were rich in protein and minerals except for the breast milk and cow milk. Thus, it is possible that a short fall in these nutrients may have constrained growth in length.

Moreover, highly prevalent childhood illnesses, particularly diarrhea in this population, might have had a negative effect on linear growth of these children (31, 35). Our results showed that morbidity during infancy was negatively associated ($P < 0.05$) with gain in weight but not with gain in length, particularly during the second half of infancy. Further research, however, is needed to confirm the association between morbidity, particularly diarrhea and linear growth in determining the lack of association between IFPs and linear growth of these children.

Despite the positive effect of IFPs on gain in weight, even the children who were most fed according to the infant feeding recommendations remained small compared with the new WHO child growth standards. There was a mean weight deficit of 0.91 kg, 1.37 kg, and 2.10 kg by 6 mo, 12 mo, and 24 mo, respectively. The attained weight of the average child at 24 mo of age was similar to that of a reference child at 12 mo of age. Similarly, the attained length of an average sample child at 24 mo of age was
similar to the same reference child at 18 mo of age. This finding indicates that there could be several other factors, such as health care, household SES, household food security, and the nutritional status of the mothers in determining growth during the first 2 y of life among these rural Bangladeshi children. This finding may also reflect that our infant feeding scales captured only a portion of the behaviors recommended for feeding infants (13, 14).

Methodologic strengths

An important strength of this study is our use of longitudinal data and statistical techniques for the analysis of longitudinal data. This approach avoided the potential problem of reverse causality that can be present in the association observed in cross-sectional studies (25, 26). As a result, findings from this study allowed us to establish a temporal relation between IFPs and growth of infants in this population.

Our infant feeding scales were based on the actual IFPs of the mothers and relative to the infant feeding recommendations. These scales, however, were not measures of food consumption but rather measures of maternal behaviors relative to the recommended behaviors. Thus, our results provide direct evidence of the importance of following the infant feeding recommendations for better growth of infants. This is a significant test of translation of infant feeding policy into maternal practice regarding infant feeding. Our feeding scales captured a part but not all aspects of the feeding recommendations, however, because we could not measure the quantity of food that children actually consumed.

We followed a novel approach for constructing the infant feeding scales with the use of longitudinal data on IFPs. Cross-sectional data were used previously to create feeding scales at different ages of infants and children (22–24). In a longitudinal study in Barbados, the investigators used an exploratory factor analysis to identify and reduce the uncorrelated factors from feeding practices of infants (20). We took the advantage of longitudinal data when we constructed our infant feeding scales that permitted us to capture the cumulative effect of feeding practices at each age.

The infant feeding scales were based on the categories of food, not on the specific food or the amount of that food that was actually offered to the infant. Therefore, we could not examine whether the variety of food offered had any effect on the growth of these children. Recent studies in Mali (36), Burkina Faso (37), and South Africa (38) confirmed the association between dietary diversity and health and nutritional outcomes for adults and children. In several other countries, height-for-age z scores for children 6–23 mo old were also associated with dietary diversity (39), which can be used as an indicator of dietary adequacy (38). In the future, it would be important to examine the association between dietary diversity and child growth in this population. This is particularly important because there is a potential of low nutrient intakes among these infants that could have resulted from low intake and low micronutrient density of complementary foods (40).

Conclusion

Findings from this study provide strong evidence to support the current infant feeding recommendations for better growth during infancy and early childhood. It is important to promote infant feeding recommendations in this population regarding portion size, feeding frequency, nutrient-dense foods, and encouragement to eat. Efforts should also be made to improve the SES and food security to ensure adequate resources and food for infant feeding and health care. Better indicators are needed to capture the multidimensional nature of infant and young child feeding. Improving IFPs may be an effective intervention to help address the burden of undernutrition in Bangladesh and similar settings elsewhere in the world.

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The authors’ responsibilities were as follows—KKS: designed the study, analyzed and interpreted the data, and drafted the manuscript; SEA, LAP, KMR, and EAF: designed the MINIMat study; KKS, DSA, SEA, and LAP: supervised data collection; EAF and KMR: supervised data analysis and interpretation. All authors contributed to the revision of the manuscript. None of the authors had a financial or personal conflict of interest.

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