

Micronutrient supplementation affects maternal-infant feeding interactions and maternal distress in Bangladesh^{1–3}

Amy L Frith, Ruchira T Naved, Eva-Charlotte Ekström, Kathleen M Rasmussen, and Edward A Frongillo

ABSTRACT

Background: Good maternal-infant interaction is essential for optimal infant growth, health, and development. Although micronutrient malnutrition has been associated with poorer interaction, the effects of maternal micronutrient supplementation on interaction are unknown.

Objectives: We examined differences in maternal-infant feeding interaction between 3 maternal pre- and postpartum micronutrient supplementation groups that differed in iron dose and inclusion of multiple micronutrients and determined whether any differences observed were mediated by maternal distress.

Design: A cohort of 180 pregnant women was selected from 3300 women in the randomized controlled trial Maternal Infant Nutritional Interventions Matlab, which was conducted in Matlab, Bangladesh. At 8 wk of gestation, women were randomly assigned to 1 of 3 groups to receive a daily supplement of micronutrients (14 wk gestation to 12 wk postpartum): 60 or 30 mg Fe each with 400 µg folic acid or multiple micronutrients (MuMS; 30 mg Fe, 400 µg folic acid, and other micronutrients). A maternal-infant feeding interaction was observed in the home when infants were 3.4–4.0 mo of age, and maternal distress was assessed.

Results: Compared with 30 mg Fe, 60 mg Fe decreased the quality of maternal-infant feeding interaction by ≈10%. Compared with 30 mg Fe, MuMS did not improve interaction but reduced maternal early postpartum distress. Distress did not mediate the effects of micronutrient supplementation on interaction.

Conclusion: For pregnant and postpartum women, micronutrient supplementation should be based on both nutritional variables (eg, iron status) and functional outcomes (eg, maternal-infant interaction and maternal distress). *Am J Clin Nutr* 2009;90:141–8.

INTRODUCTION

Verbal and nonverbal maternal-infant interaction underlies infant growth, health, and development (1) and is an integral part of the infant feeding process (2). The quality of maternal-infant interaction may be compromised by deficiencies in pregnant and lactating women of micronutrients necessary for fetal development (3) and maternal mental health (4, 5). The influence of different maternal micronutrient supplements on maternal-infant interaction has not been established. Given the high prevalence of micronutrient deficiencies in developing countries (6), the potential effect on maternal-infant interaction is considerable.

Anemia due to iron deficiency is prevalent in pregnant women worldwide (51%) (7). Iron deficiency and anemia are detrimental to fetal development (8), infant responsiveness (9), and maternal

mental health (10, 11), which affect maternal-infant interaction (12, 13). Iron supplementation of anemic mothers from 10 wk to 9 mo postpartum reduced depression (10) and improved maternal-infant interaction (12).

The optimal dose of iron supplements for pregnant women is debatable (6, 14–16). Higher iron doses can result in side effects (17), which can result in reduced supplement consumption (18) or continued consumption of supplement despite feeling poorly (19). Mothers who reduce their iron intakes or are sick may interact poorly with their infants (20). Understanding the influence of iron dose on maternal-infant interaction and maternal distress will contribute to resolving this debate.

Another issue is whether supplementation with multiple micronutrients is preferable to supplementation with iron and folic acid alone. Women in developing countries often have several micronutrient deficiencies simultaneously (6). Many micronutrient deficiencies are associated with poorer quality of maternal-infant interaction (21, 22) and mental health of mothers (4, 5). Multiple micronutrient supplementation may benefit

¹ From Cornell University, Division of Nutritional Sciences, Ithaca, NY (ALF); ICDDR,B: Centre for Health and Population Research, Dhaka, Bangladesh (RTN); Uppsala University, Women's and Children's Health, International Maternal and Child Health, Uppsala, Sweden (E-CE); Cornell University, Division of Nutritional Sciences, Ithaca, NY (KMR); and the University of South Carolina, Department of Health Promotion, Education, and Behavior, Columbia, SC (EAF).

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³ Address correspondence to EA Frongillo, Department of Health Promotion, Education, and Behavior, University of South Carolina, Columbia, SC. E-mail: efrongillo@sc.edu.

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maternal-infant interaction by addressing many nutrient deficiencies simultaneously or by improving the bioavailability of iron supplementation (23, 24). Conversely, simultaneous administration of iron with other micronutrients can interfere with iron absorption or utilization in iron-replete individuals (25).

We carried out a randomized double-blind controlled trial in a rural community in Bangladesh to examine the effect of daily micronutrient supplements (30 mg Fe compared with 60 mg Fe, or 30 mg Fe iron compared with multiple micronutrients) in pregnant and early postpartum mothers on observed maternal-infant feeding interaction when infants were 3.4–4.0 mo of age. In a previous study of this community, 23% of the women were anemic (26), and other micronutrient deficiencies were likely common because the women consume diets with inadequate levels of energy, iron, zinc, and B vitamins (27, 28).

SUBJECTS AND METHODS

Subjects and study design

This study was conducted between June 2003 and January 2004 in 2 subcenter areas in Matlab, a subdistrict of the Chandpur district that is typical of the rural and riverine delta of Bangladesh (29). The women and children residing here receive free maternal and child health care from the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), Centre for Health and Population Research. Written informed consent was obtained from each woman before enrollment. The institutional review boards of ICDDR,B and Cornell University approved the study protocol.

This study was part of a larger study, Maternal and Infant Nutritional Interventions, Matlab (MINIMat). MINIMat was a randomized, double-blind, controlled field trial with a $3 \times 2 \times 2$ factorial design. Pregnant women at 8 wk of gestation were randomly and independently assigned to receive 1 of each of the 3 nutritional interventions. Beginning at 14 wk of gestation, each participant received a daily micronutrient supplementation of either 60 mg or 30 mg Fe with 400 μ g folic acid or multiple micronutrients (MuMS; 30 mg Fe with the UNICEF formulation) (30) (Table 1). Each participant was assigned to a food supplementation group, either promotion to an “early” start of daily food supplementation (600 kcal/d; 6 d/wk), commonly during the first trimester, or no such promotion, which is the “usual” start of participation in the governmental program (commonly during the second trimester) until giving birth. Every participant was also assigned to receive 1 of 2 counseling protocols from 30 wk of gestation until 6 mo after giving birth. Participants received either health counseling alone or health counseling with exclusive breastfeeding counseling. For this article, all interventions other than the micronutrient supplementation were ignored after we established that, in our subset of women, they did not influence the relation between the type of micronutrient supplementation and maternal-infant interaction during feeding.

Maternal characteristics, including parity, age, education, socioeconomic status, food insecurity, and height and weight during early pregnancy were assessed by questionnaire at 8–10 wk of gestation. Maternal hemoglobin was assessed by using Hemocue at 14 and 30 wk of gestation. A wealth index was used

TABLE 1

Composition of multiple micronutrient supplements (30) administered daily to Bangladeshi women ($n = 55$) in the Maternal Infant Nutritional Interventions Matlab study during pregnancy and the early postpartum period (14 wk gestation until 3 mo postpartum)

Nutrient	Amount
Vitamin A (μ g)	800
Vitamin D (IU)	200
Vitamin E (mg)	10
Vitamin C (mg)	70
Thiamine (mg)	1.4
Riboflavin (mg)	1.4
Niacin (mg)	18
Vitamin B-6 (mg)	1.9
Vitamin B-12 (mg)	2.6
Folic acid (μ g)	400
Iron (mg)	30
Zinc (mg)	15
Copper (mg)	2
Selenium (μ g)	65
Iodine (μ g)	150

to assess socioeconomic status based on a composite of information about land ownership, characteristics of the household dwelling, and household ownership of durables (ie, bed, quilt, mattress, watch/clock, chair/table, cabinet, bicycle, radio, television, electric fan, cows, goats, and chicken/ducks) (31). Questionnaires were used to obtain information about the experience of side effects, including symptoms of reduced appetite and strength or an increase in fever, heartburn, nausea, loose stool, dizziness, constipation, dark stools, vomiting, headache, bad taste in mouth, or stomachache at 18 wk of gestation. Infant characteristics were collected within the first 7 d of birth for the vast majority of infants and within 30 d of birth for a few infants.

The subsample for this study was recruited from all 202 eligible MINIMat participants who gave birth between May and October 2003 in 2 of the 4 health center areas. MINIMat participants were eligible if they had an infant between 3.4 and 4.0 mo of age who was free of obvious congenital anomalies.

Of the 202 mother-infant dyads that were recruited, 180 were observed for maternal-infant feeding interaction. Twenty-two did not participate because 2 infants were ill, 2 mothers refused to participate, and 18 mothers were not at home when the infant was the correct age.

Micronutrient supplements

The supplements were provided as individual doses of pills that were indistinguishable from one another. The mothers' compliance during the prenatal period was measured by monitoring the intake of micronutrient supplements by using microchip technology that recorded how many times a pill bottle had been opened and closed during a specified time period. The MuMS supplement used in this trial contained micronutrient doses based on the American and Canadian recommended daily allowance, except for the folic acid dose, which was set at 400 μ g (32–34). The current recommendation in Bangladesh is to supplement pregnant women with 60 mg Fe and 400 μ g folic acid.

Maternal-infant feeding interaction

The first author was trained and certified by using standard procedures (reliability >90% compared with standard scoring with videotaped scenarios) to use the Nursing Child Assessment Satellite Training Feeding Scale (NCAST) by a certified NCAST trainer (Mary Byrne, Columbia University School of Nursing, New York, NY) (35). The first author measured maternal-infant feeding interaction on a single day in the participant's home. A Bengali researcher assisted in recording maternal verbalizations. All feeding interactions were observed before the interviews to avoid influencing the feeding interactions. The researchers minimized the effect of the observation on feeding behavior by living in the study community, having familiar local health community workers introduce them, and developing a rapport with the mother and family through home visits before observing interactions.

The underlying concepts used in NCAST are based on attachment, developmental psychology, and psychobiology literature. NCAST is a well-known observation tool that is used to assess the quality of maternal-infant interaction in both clinical and research settings. NCAST is used to identify infants at risk of developmental delays and to measure the effects of interventions on quality of interaction. The behaviors of a mother and infant dyad are observed during feeding, and observations are recorded on a scale. This scale is composed of 76 behavioral descriptions of the mother, infant, or both. Behaviors are scored "1" if they occur and "0" if they do not occur. The number of behaviors observed is summed. Higher scores indicate a better quality of interaction. Total, mother, and infant total and 7 subscale behavioral scores represent the quality of the maternal-infant dyadic interaction. The total score is a composite of maternal and infant scores. The maternal score comprises 4 subscales: sensitivity, response to infant distress, social emotional growth fostering, and cognitive fostering. The infant score comprises 2 subscales: clarity of cues and responsiveness to caregiver. In addition, the NCAST feeding scale can be used to determine whether the mother has exhibited positive behaviors (eg, smiling, eye contact, touching gently, and positive verbalization) or negative behaviors (eg, frowning, pursing the lips, shaking, hitting, shouting, or negative verbalizations) toward the infant.

The major concepts imbedded in the NCAST feeding scale are contingency, positioning, verbalness, sensitivity, affect, and engagement/disengagement. Contingency is measured by observing whether the mother or infant responds to the actions of the other within a short period of time. Proper positioning of the infant's head and body during breastfeeding is assessed because it is important for feeding interaction. Verbalness refers to the presence or absence of the mother speaking to the infant, whether it is positive or negative in tone and intent and of the infant either crying or producing other nonfeeding noises. Sensitivity measures whether the mother responds appropriately to the infant's engagement or disengagement cues. Affect is measured by observing the positive or negative facial expressions of the mother and infant. Infant engagement/disengagement cues are specifically defined and represent behaviors that indicate if the infant wants to begin, end, or change the feeding situation. The NCAST manual includes a detailed summary of reliability and validity information (35). Reliability and validity of the NCAST in Bangladesh was described previously (36). In brief, total, ma-

ternal, and infant NCAST scores in mother-infant dyads in Bangladesh did not differ from the norms in the United States for other ethnic groups with low education and adolescents (35, 37). The NCAST scores were correlated (Pearson, 0.44; $P < 0.001$) with the Mother-Infant Communication Screening (MICS) scores in the study Bangladeshi population. These 2 instruments have similar theoretical foundations (37). Two Bengali researchers scored the MICS during nonfeeding episodes, and the first author scored the NCAST during feeding episodes on a different day. The researchers did not discuss the scores and were blinded to treatments. The Kuder-Richardson formula was used to measure internal consistency for NCAST: NCAST total score (0.85; 76 items), maternal total score (0.68; 50 items), and infant total score (0.86; 26 items) (38).

Distress

On the day after the feeding interaction was assessed, 1 of the 2 research assistants interviewed the mothers using the self-reporting questionnaire SRQ-20 (39) to assess distress (40). The SRQ-20 is a 20-item questionnaire that prompts "yes" and "no" responses and was designed to identify "mental distress" in individuals within a community. To assess distress, the SRQ-20 includes items to assess depressive and anxiety symptoms and includes physical symptomatology that is often associated with depression and anxiety in non-Western cultures. Some symptoms of depression included items pertaining to feelings of worthlessness, unhappiness, and not being able to enjoy activities. Examples of the symptoms of anxiety included items pertaining to feeling tired, having stomach problems, and being easily frightened. Scores range from 0 to 20, with a higher score indicating more distress.

The reliability and validity of the SRQ-20 has been established in 6 countries (39). We used the Kuder-Richardson formula to determine the internal consistency, which was 0.84 (38). The questionnaire was field-tested with 30 pregnant women in this community; women were asked to explain their responses in a separate cognitive interview to check whether their understanding of the questions matched with our understanding (41). Bilingual research assistants translated and back-translated the Bengali version of the interview protocol.

Data analysis

Data were recorded in the field on pretested forms and were checked by the supervisor before and after the data were entered into computers. Analyses were done by using SPSS software (version 16; SPSS Inc, Chicago, IL). Univariate analysis was used to identify outliers, which were then checked against the original field forms and resolved. We used the NCAST feeding interaction score as the primary outcome measure for evaluating the effects of micronutrient supplementation on maternal-infant interaction during feeding. NCAST scores were reported as means \pm SDs.

Each participant received one type of food supplementation intervention and one type of counseling intervention. To examine whether the effect of micronutrient supplementation on maternal-infant interaction was modified by food supplementation, we introduced the interaction term of micronutrient supplement and food supplement groups using analysis of variance. We found that the interaction term was not significant ($P = 0.83$). We did the

same for micronutrient supplement and counseling interventions and found that the interaction term was not significant ($P = 0.51$). In addition, the distribution of the sample among food supplementation and counseling groups was equivalent across micronutrient groups. As a result, we analyzed the main effects of micronutrient supplements across the combined food supplement and counseling intervention groups.

To determine whether baseline values of demographic and health characteristics and whether micronutrient supplement intakes differed between those who participated in the study and those who did not, we used t tests for continuous variables and chi-square analysis for categorical variables. In this subset, we examined whether baseline demographic and health characteristics differed between the 3 micronutrient supplementation groups using a one-factor analysis of variance.

We conducted a one-factor analysis of variance, with a priori linear contrasts, to examine if MuMS improved maternal-infant interaction during feeding compared with 30 mg Fe with 400 μg folic acid and to examine whether 60 mg Fe with 400 μg folic acid had a different effect on maternal-infant interaction during feeding than did 30 mg Fe with 400 μg folic acid. To compare the SDs of maternal-infant interaction for the 30-mg and 60-mg Fe groups, we used an F test. We did not control for covariates because the means of all demographic and health variables did not differ according to micronutrient supplementation in this subset. Furthermore, we did not control for the number of supplements taken (measured by number of times the supplement bottle was opened) because, in this subset of women, there were no significant differences between groups with type of micronutrient supplement ($P = 0.221$); the intake of number of pills was measured as 78.4, 72.3, and 66.0 for the 30-mg Fe, 60-mg Fe, and MuMS groups, respectively. Also, we did not control for iron status. Because serum ferritin was assessed in only a portion of the main MINIMat study sample, we had available serum ferritin values for 56 of 180 women at 14 wk of gestation. In our subset, there were no significant differences with type of micronutrient supplement ($P = 0.371$); the mean serum ferritin concentrations were 47.8, 38.0, and 47.2 ng/mL for the 30-mg Fe, 60-mg Fe, and MuMS groups, respectively. To examine whether the effect of micronutrients on feeding interaction differed according to concentration of initial maternal hemoglobin (14 wk of gestation), the concentration of hemoglobin at 30 wk of gestation, or the change in concentration of hemoglobin over pregnancy, we introduced the interaction term of the micronutrient supplement groups and each hemoglobin measure separately using analysis of variance. We used analysis of variance to determine whether side effects were related to the quality of maternal-infant interaction.

To test whether distress mediated the effects on the interaction, we used a one-factor analysis of variance, with a priori linear contrasts, to examine whether MuMS or 60 mg Fe with 400 μg folic acid influenced early postpartum distress compared with 30 mg Fe with 400 μg folic acid. We then added distress to the general linear model that related micronutrient groups and feeding interaction (42).

The power for detecting differences between micronutrient groups was determined by selecting $\alpha = 0.05$, with a sample size of 55 for each group and 2-tailed tests. There was a power of ≥ 0.80 to detect a difference of 2.5 in total NCAST scores (43) between groups. The difference of 2.5 in NCAST scores is ap-

proximately the difference observed when comparing children with and without physical handicaps or the difference observed when comparing mothers with low compared with high levels of education in the United States. To be conservative, we used 2-tailed tests, although we hypothesized that MuMS would improve maternal-infant interaction during feeding compared with 30 mg Fe and 400 μg folic acid.

RESULTS

Maternal and infant characteristics

Mother's parity, age, education, socioeconomic status, and body mass index (BMI) did not differ significantly between those who did not participate in the present study and the study sample, and these variables were similar to those of the larger population of MINIMat participants (data not shown). There were no differences between micronutrient supplement groups in maternal or infant (ie, sex) characteristics at the beginning of the study (Table 2), including concentration of hemoglobin at 14 wk. Furthermore, in this subset of women, there was no difference in the number of pills taken (data not shown). There were no significant differences in the initial characteristics between this subsample and the larger MINIMat sample (data not shown).

TABLE 2

Baseline demographic characteristics of Bangladeshi mothers and infants (3.4–4.0 mo of age) in the Maternal Infant Nutritional Interventions Matlab (MINIMat) study by daily maternal micronutrient supplement intake (14 wk gestation until 3 mo postpartum)

Baseline characteristic	Supplement group ¹		
	30 mg Fe (n = 58)	60 mg Fe (n = 67)	MuMS (n = 55)
Mother			
Parity	1.5 ± 1.3 ²	1.3 ± 1.3	1.8 ± 1.7
Age (y)	27.1 ± 5.3	25.6 ± 6.0	27.5 ± 7.0
Education (y)	7.2 ± 3.2	6.6 ± 3.3	6.7 ± 2.4
BMI (kg/m ²)	19.6 ± 2.7	19.5 ± 2.6	19.7 ± 2.4
Wealth index (%)³			
1 (poorest)	27.9	23.3	25.6
2	18.6	20.9	19.8
3	12.8	20.9	15.1
4	20.9	12.8	17.4
5 (wealthiest)	19.8	22.1	22.1
Location (%)⁴			
A Block	63.6	56.9	55.8
C Block	36.4	43.1	44.2
Infant female sex (%)	56.9	53.7	54.4

¹ No significant differences ($P < 0.05$) were found between micronutrient groups [30 mg Fe with 400 μg folic acid, 60 mg Fe with 400 μg folic acid, and multiple micronutrients (MuMS, 30 mg with 400 μg folic acid and other micronutrients)] by ANOVA.

² Mean ± SD (all such values).

³ The wealth index assessed socioeconomic status based on a composite of information about land ownership, characteristics of the household dwelling, and household ownership of durables (ie, bed, quilt, mattress, watch/clock, chair/table, cabinet, bicycle, radio, television, electric fan, cows, goats, and chicken/ducks).

⁴ The subsample for this study was recruited from all eligible MINIMat participants who gave birth between May and October 2003 in 2 of the 4 health center areas (referred to as block A and block C).

There were no differences in maternal or infant characteristics between those who participated in this study and those who did not participate in this study (data not shown).

Maternal-infant interaction

There were no differences in NCAST feeding scores between the 30-mg Fe and MuMS groups and no differences between the 60-mg Fe and MuMS groups. The 60-mg Fe group had lower NCAST scores than did the 30-mg Fe group for total ($P = 0.015$), maternal ($P = 0.039$), and infant ($P = 0.008$) scores (Table 3). The 60-mg Fe group had lower NCAST scores than did the 30-mg Fe group for maternal sensitivity ($P = 0.006$), and, for both infant subscales, clarity of cues ($P = 0.028$) and responsiveness to caregiver ($P = 0.007$). The 60-mg Fe group tended to have lower NCAST scores than did the 30-mg Fe group for maternal socioemotional fostering ($P = 0.074$) and maternal cognitive fostering ($P = 0.100$). Besides the 60-mg Fe group having lower mean total NCAST scores than the 30-mg Fe group, the 60-mg Fe group had a larger SD as tested by an

F test, which indicated that the width of the distribution of maternal-infant feeding interaction scores was altered ($P = 0.002$).

Not only were the feeding interaction scores lower in the 60-mg Fe group, but the quality of maternal behaviors differed from the 30-mg Fe group. In the 60-mg Fe group, the percentage of mothers who exhibited one or more negative behaviors was higher ($P = 0.030$, chi-square test), and the percentage of mothers who exhibited one or more positive behaviors was lower ($P = 0.010$) than in the 30-mg Fe group (Table 3).

Distress

The MuMS group had a lower mean (\pm SD) distress score than did the 30-mg Fe group (6.2 ± 4.0 and 9.0 ± 5.1 , respectively; $P = 0.041$). There were no statistically significant differences between the MuMS and the 60-mg Fe groups (mean \pm SD; 6.2 ± 4.0 and 7.3 ± 4.6 , respectively; $P = 0.169$) or between the 30-mg and 60-mg Fe groups. Although the micronutrient groups affected both distress and feeding interaction, distress did not mediate the effects of micronutrient groups on feeding interaction when distress was added to the general linear model for feeding interaction ($P > 0.05$).

TABLE 3

Effect of daily maternal micronutrient supplements (14 wk gestation until 3 mo postpartum) on maternal-infant feeding interaction (Nursing Child Assessment Satellite Training; NCAST) scores and the percentage of mothers exhibiting positive or negative behaviors during feeding among Bangladeshi mothers and infants (3.4–4.0 mo of age) in the Maternal Infant Nutritional Interventions Matlab study

	Supplement group ¹		
	30 mg Fe (<i>n</i> = 58)	60 mg Fe (<i>n</i> = 67)	MuMS (<i>n</i> = 55)
Feeding behavior			
Feeding interaction			
Total NCAST ²	56.4 \pm 8.8 ^{3,4}	51.7 \pm 12.8	54.1 \pm 9.3
Mothers			
Total	36.4 \pm 6.5 ⁴	33.5 \pm 9.4	35.3 \pm 6.9
Sensitivity	12.8 \pm 2.2 ⁴	11.7 \pm 2.6	12.3 \pm 2.1
Response to infant distress	8.7 \pm 1.9	8.5 \pm 2.2	9.0 \pm 1.9
Socioemotional fostering	9.2 \pm 2.6	8.2 \pm 3.5	8.7 \pm 2.5
Cognitive fostering	5.8 \pm 2.0	5.1 \pm 2.4	5.4 \pm 2.5
Infants			
Total	20.0 \pm 3.0 ⁴	18.2 \pm 4.2	18.8 \pm 3.6
Clarity of cues	13.1 \pm 1.5 ⁴	12.3 \pm 2.3	12.6 \pm 2.1
Responsiveness to caregiver	6.9 \pm 1.8 ⁴	5.9 \pm 2.2	6.2 \pm 1.8
Mothers (%)			
≥ 1 Negative behavior ⁵	25.9 ⁶	44.8	25.5
≥ 1 Positive behavior ⁷	98.3 ⁶	89.6	100.0

¹ Supplement groups [30 mg Fe with 400 μ g folic acid, 60 mg Fe with 400 μ g folic acid, and multiple micronutrients (MuMS, 30 mg with 400 μ g folic acid and other micronutrients)].

² Total NCAST scores reflect the combination of total subscale score of the mothers and infants.

³ Mean \pm SD (all such values).

⁴ Significantly different from 60 mg Fe by a priori linear contrasts, $P < 0.05$.

⁵ Negative behaviors, such as frowning, pursing the lips, shaking, hitting, shouting, or negative verbalizations to the infant.

⁶ Significantly different from 60 mg Fe by a priori chi-square tests, $P < 0.05$.

⁷ Positive behaviors, such as smiling, eye contact, touching gently, and positive verbalization to the infant.

DISCUSSION

MuMS during pregnancy and the early postnatal period did not improve the quality of maternal-infant interaction compared with 30 mg Fe and 400 μ g folic acid or 60 mg Fe and 400 μ g folic acid. In addition, a higher dose of iron (60 mg Fe and 400 μ g folic acid) was detrimental to maternal-infant interaction when compared with a lower dose of iron (30 mg Fe and 400 μ g folic acid). Although MuMS reduced early postpartum distress in mothers compared with 30 mg Fe and folic acid alone, distress did not mediate the effects of micronutrients on interaction. One formulation (ie, MuMS) benefited mothers by reducing distress, whereas another formulation (ie, 30 mg Fe and 400 μ g folic acid) benefited mothers and infants by enhancing maternal-infant interaction.

Possible reasons that additional multiple micronutrients did not benefit maternal-infant interaction compared with 30 mg or 60 mg Fe include the following: 1) participants did not experience multiple micronutrient deficiencies, 2) low doses of the micronutrients (ie, recommended daily dietary allowance) were not sufficient to influence fetal development, 3) other micronutrients besides iron have little influence on infant or maternal behavior, and 4) the NCAST feeding scale may not have captured specific affected behaviors. The study participants likely had multiple micronutrient deficiencies, because women in rural Bangladesh consume diets low in micronutrients (28). Perhaps the low dose of micronutrients present in the MuMS preparation was insufficient to influence fetal development in a malnourished population. In one study, 25 mg Zn/d during pregnancy influenced fetal behavior (44). In our study, 15 mg Zn/d may have been insufficient to alter fetal development or behavior.

That micronutrients other than iron may have little influence on infant behavior seems unlikely because many micronutrients are necessary for normal fetal development (6). Previous human and animal studies indicate that micronutrient deficiencies (eg, zinc and vitamin B-6) are related to specific infant behaviors (eg,

the amount of vocalization) (45–47, 21, 22). Further investigation should examine whether various doses of micronutrients affect maternal-infant interaction, specific infant behavior and development, and maternal and infant iron status.

That the higher dose of iron reduced the quality of feeding interaction compared with the lower dose of iron may have occurred because of reduced maternal plasma zinc concentrations, increased maternal or infant morbidity, or increased maternal side effects. Higher doses of iron may reduce the concentration of zinc, which leads to poorer maternal-infant interaction (22). Iron inhibits zinc absorption when administered together in an aqueous solution (48). Daily consumption of 60 mg Fe during pregnancy reduced the concentrations of zinc in blood and milk after delivery (49). Inasmuch as zinc is essential for normal fetal development (50), poor maternal zinc status may affect the behavior of infants negatively and be detrimental to the interaction.

The higher dose of iron may have reduced the quality of interaction by increasing maternal morbidity, especially in iron-replete individuals. Increased morbidity may be due to reduced immunity or increased bacterial virulence (51, 52). Parenteral iron supplementation increases the incidence of malaria, diarrhea, and tuberculosis (53–55). The higher dose of iron could have also increased oxidative stress and compromised placental function, leading to poor fetal development (56). In our study, however, the effect of micronutrient supplementation on the interaction did not differ with concentration of hemoglobin during pregnancy. We could not assess whether the higher dose of iron increased morbidity.

Another explanation is that 60 mg Fe may have produced side effects in mothers that reduced the quality of interaction. The quality of maternal-infant interaction is established in the first month postpartum and is stable thereafter (35). If mothers experienced postpartum gastrointestinal problems with the 60-mg Fe supplements, they may have interacted less well with their infants. In this subset, side effects were unrelated to maternal-infant interaction, so this is not a likely mechanism by which a higher dose of iron reduced the quality of interaction.

MuMS reduced distress compared with 30 mg Fe. Micronutrient deficiencies (ie, zinc, thiamine, and folate and low hemoglobin concentrations) are associated with poor mental health (4, 11, 57, 58), and single micronutrient supplementation (ie, zinc, folic acid, and vitamin B-12) can relieve symptoms of distress (57, 59) through an influence on neurotransmitters (60). A therapeutic dose of iron supplements in anemic mothers from 10 wk to 9 mo postpartum relieved depression and stress (10). Our study suggests that, in a community-based intervention, the addition of multiple micronutrients to 30 mg Fe may improve the well-being of malnourished women.

Distress did not mediate the effects of micronutrients on maternal-infant interaction during feeding because distress was not related to interaction. Poor maternal psychological functioning is detrimental to the quality of maternal-infant interaction (61, 62). Iron supplementation to anemic mothers reduces depression and stress (10), and other micronutrients are associated with mental health. We proposed that the different treatment groups, with their different doses of iron and the addition of multiple micronutrients, would reduce distress to different extents and thereby improve maternal-infant interaction to different extents. Maternal distress may have to be reduced more

than that observed in this study to effect an improvement in quality of maternal-infant interaction. Furthermore, the strong relation between maternal depression and poor maternal-infant interaction that is observed in Western societies may be less straightforward when undernutrition also influences interaction (63). Undernutrition is highly prevalent in the study area with 30% of infants born with birth weight <2500 g and infants having average deficits of 910 g in weight and 3.2 cm in length at 6 mo relative to World Health Organization standards (64). Maternal-infant interaction is influenced by context (ie, maternal social support) and maternal and infant characteristics (ie, health and infant temperament) in Western societies (1). Although different micronutrient formulations may have affected infant health, maternal health, or infant temperament, these factors may have modified the effect of micronutrient supplementation on maternal-infant interaction. For example, 60 mg Fe may have most affected maternal-infant interaction in infants with a difficult temperament (ie, fussy, hard to soothe, negative affect, and irregular sleep and eating patterns). More research is needed to understand how nutritional, psychological and social factors influence maternal-infant interaction, particularly where mothers are undernourished.

High-quality maternal-infant feeding interaction and good maternal psychological functioning are beneficial to infant development and to maternal health, so the type of micronutrient supplement that pregnant and lactating women consume likely has long-term implications for the well-being of mothers and their children. Currently, public health programs deliver either 60 or 30 mg Fe supplements to pregnant and/or postpartum women, in part, based on the prevalence of anemia. Recommendations for micronutrient supplementation should be formulated considering effects on both nutritional variables (eg, iron status) and functional outcomes (eg, maternal-infant interaction and maternal distress). The optimal supplement depends on the desired outcomes for both the mother and her infant.

The MINIMat team designed the MINIMat study, recruited the subjects, and carried out the interventions under the leadership of Lars Åke Persson and Shams El Arifeen. BRAC carried out the food supplementation distribution. In Matlab, M Shahidullah supervised the intervention and the data collection. We gratefully acknowledge the participation of all pregnant women and families in Matlab and Mary Byrne of Columbia University School of Nursing (New York, NY) for the NCAST training she provided.

The authors' responsibilities were as follows—ALF: collected and analyzed the data; and EAF: analyzed the data. All authors contributed to the design and reporting of the study. None of the authors had any financial or personal interest in any company or organization sponsoring the research.

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