

# Iron deficiency and child and maternal health<sup>1–4</sup>

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## ABSTRACT

**Background:** Iron deficiency is most commonly found in women of reproductive age and infants worldwide, but the influence of maternal iron deficiency on infant development is underexplored.

**Objective:** The objective was to examine the relation between maternal iron status and mother-child interactions in a randomized, double-blind, intervention trial conducted in South Africa.

**Design:** Women were recruited into the study from a health clinic at 6–8 wk postpartum and were classified as either iron-deficient anemic (IDA) or iron-sufficient after blood analysis. IDA mothers received iron supplements of 125 mg FeSO<sub>4</sub> (IDA-Fe; *n* = 34) or placebo (IDA-PL; *n* = 30) daily from 10 wk to 9 mo postpartum. The control group (*n* = 31) consisted of iron-sufficient mothers. Free-play mother-child interaction sessions were videotaped in the clinic at 10 wk (*n* = 80) and 9 mo (*n* = 66) postpartum and coded per the Emotional Availability Scales (4 maternal scales: sensitivity, structuring, nonintrusiveness, and nonhostility; 2 infant scales: responsiveness and involvement).

**Results:** At 10 wk, scores for maternal sensitivity and child responsiveness were significantly greater in the control group than in the IDA groups (*P* = 0.028 and 0.009, respectively). At 9 mo, the control and IDA-Fe groups no longer differed. These 2 groups scored significantly better on the maternal sensitivity, structuring, and nonhostility scales and on the child responsiveness scale than did the IDA-PL group (*P* = 0.007–0.032), whose iron status remained low.

**Conclusion:** These data indicate that maternal iron deficiency negatively affects mother-child interactions and that iron supplementation protects against these negative effects. *Am J Clin Nutr* 2009;89(suppl):946S–50S.

## INTRODUCTION

Iron deficiency is the most prevalent single nutrient deficiency in the world (1) and is recognized by the World Health Organization as 1 of the 10 greatest global health risks in existence today (2). Anemia affects the lives of >2 billion people worldwide and twice as many are iron-deficient (2). Worldwide, 50% of women of reproductive age are iron-deficient, with estimates as high as 80% in pregnant women from developing countries. **Recovery of iron stores in the postpartum period is often delayed in women who experienced iron deficiency anemia during pregnancy.**

The consequences of iron deficiency include reduced physical work capacity, poor immune function, and changes in cognition, emotions, and behavior. The bulk of the research has been conducted in infants and young children, and most studies have

reported altered mental and motor development in iron-deficient-anemic children (3–5). Research in infants also suggests that iron-deficient infants are less attentive and more wary, clingy, and hesitant than are their non-iron-deficient counterparts (5). Whereas most research has focused on young children, altered cognition and behavior have been investigated in iron-deficient women of reproductive age (6–11). Behavioral symptoms associated with iron deficiency in adults include irritability, apathy, fatigue, depressive symptoms, and hypoactivity. Although data are beginning to emerge on the relation between iron status, cognition, and behavior in women of reproductive age, there is a relative lack of information regarding the influence of maternal iron deficiency during the postpartum period on infant development. Modifications in a mother's emotional and cognitive functioning may alter mother-child interactions, which, in turn, may affect infant behavior and development. Two reports on the outcomes of this study in a settlement community outside of Cape Town, South Africa, have been published (11, 12). The current study used the Emotional Availability Scales (EAS) to reexamine mother-child interactions. We decided to reevaluate mother-child interactions with the EAS for several reasons. Unlike most other scales, the EAS is geared specifically toward research. It has 3 underlying assumptions that ensure that the mother and child are treated as a dyad rather than as 2 individuals acting independently, that the child's developmental level is considered, and that the context is considered when evaluating the interaction. We believe that these 3 concepts are crucial when evaluating the relation between a nutrient deficiency and mother-child interactions. Additionally, given the differences in affect between the iron-deficient-anemic and control mothers in this study (11), we hypothesized that the iron-deficient-anemic mothers would be less emotionally available to their infants than would be the control mothers. The EAS consists of 6 dimensions of emotional regulation in the dyad; 4 of

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these dimensions address the emotional availability of the mother and 2 the emotional availability of the child. The new information provided us the opportunity to examine in much greater detail the degree to which maternal undernutrition alters the mother's ability to facilitate, scaffold, and organize the child's play. A previous study by Perez et al (12) used the Parent Child Interaction Scale and provided the general description of mother-child interactions in iron-deficient mothers but lacked the detail provided by the EAS.

## SUBJECTS AND METHODS

### Setting

This study was conducted in Khayelitsha, South Africa, which is a settlement community located 40 km east of Cape Town; at the time of the study, this community was home to  $\approx 400,000$  individuals. This community has water and electricity but most homes have neither.

### Design

This study was part of an investigation using a randomized, placebo-controlled, double-blind, intervention design to investigate in the postpartum period the relation between maternal iron status and measures of maternal cognition, emotional state, child development, and mother-child interaction (11, 12). The current report focuses on the mother-child interaction outcome. The details of the design and subject criteria are elaborated elsewhere (11) but are also summarized below. The study involved 3 groups of mothers: iron-deficient-anemic mothers who were given a placebo daily consisting of 25 mg vitamin C and 10  $\mu\text{g}$  folic acid (IDA-PL); iron-deficient-anemic mothers who were given a daily dose of 125 mg  $\text{FeSO}_4$ , 25 mg vitamin C, and 10  $\mu\text{g}$  folic acid (IDA-Fe); and nonanemic control mothers who received no supplementation.

The inclusion and exclusion criteria were as described below. IDA women had a hemoglobin concentration between 90 and 115 g/L and  $\geq 2$  of the following iron-deficiency markers: mean corpuscular volume  $< 80$  fL, transferrin saturation  $< 15\%$ , and serum ferritin  $< 12$   $\mu\text{g/L}$ . Any woman with a hemoglobin concentration  $< 90$  g/L was excluded from the study as being too anemic and was referred to treatment and provided iron supplements. We used C-reactive protein as an indicator of immune system activation; when the values were  $> 5.0$  mg/L, ferritin was no longer used as a criterion of iron-deficiency anemia because it can be falsely elevated during inflammation. Control subjects had to have a hemoglobin concentration  $> 135$  g/L, a mean corpuscular volume  $> 80$  fL, transferrin saturation  $> 15\%$ , and a serum ferritin concentration  $> 12$   $\mu\text{g/L}$ . Mothers had to be between 18 and 30 y of age, be the primary caregivers, be breastfeeding for the duration of the study, have no chronic diseases, and be apparently healthy at the physical health screening. None of the mothers was positive for HIV; however, HIV testing was performed as part of a government project and was not part of our inclusion or exclusion criteria. The infants had to be  $> 38$  wk of gestational age at birth, have a birth weight  $> 2500$  g, not have been hospitalized during the neonatal period, and have Apgar scores  $> 7$  (consistent with normal intrauterine growth and development).

### Recruitment

Participants were recruited during their 6-wk postpartum well-baby visit at one of the health clinics in Khayelitsha. A detailed explanation of the study was given to each woman in her native language, Xhosa, and informed consent was obtained at that time either through a signature or a symbol of affirmation. Measures reported at this time were collected at 2 time points: 10 wk postpartum and 9 mo postpartum.

### Measures

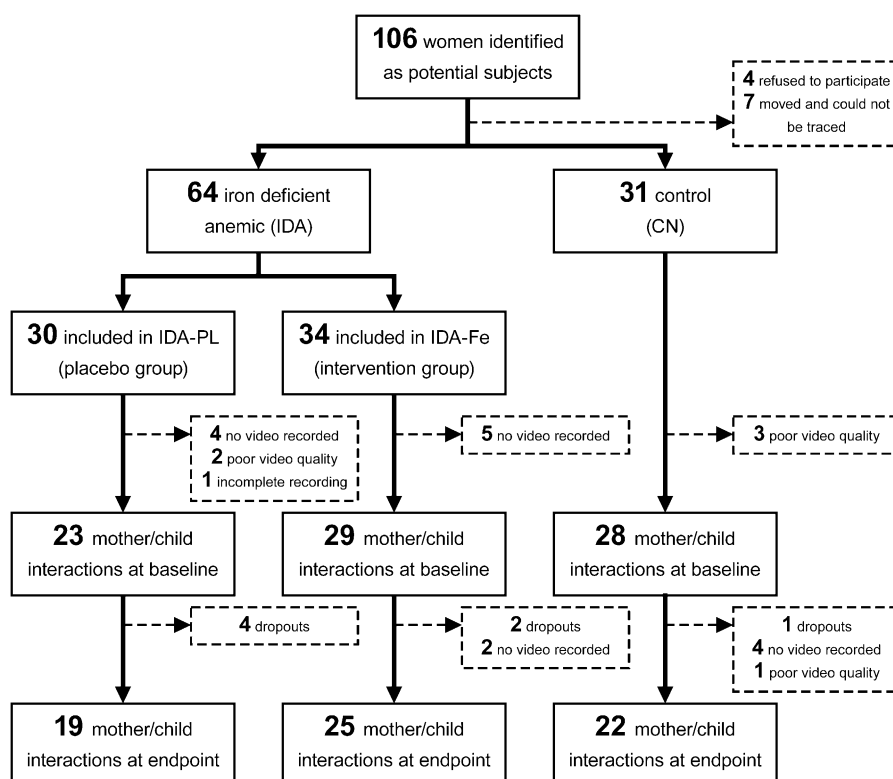
Details of the mother-child interaction methods are provided. (For a detailed explanation of the outcome measures, see reference 11.) Mother-child interactions were recorded during 20 min of free play in the health clinic at the 10-wk and 9-mo visits. During these sessions, mothers were provided with a basket of age-appropriate toys and were given no instructions other than being told that they should not allow their child to sleep during the 20 min of filming and that they should try to interact with their infant in a fashion that was typical of their daily interactions. There were no other persons in the room during the videotaping sessions. Each videotape was viewed and coded independently by 2 trained coders who were blind to all other data. Interactions were coded with the use of Biringen's EAS (13), which codes 4 maternal scales (sensitivity, structuring, nonintrusiveness, and nonhostility) and 2 child scales (responsiveness and involvement (this scale was only scored at the 9-mo time point because the 10-wk-old infants were too young to display enough variability on this scale)). Interobserver reliability was adequate (90%). A higher score on each of the scales is indicative of more optimal behavior. All methods were reviewed and approved by the Institutional Review Board at the Pennsylvania State University and the University of Cape Town and were in accordance with the Helsinki Declaration of 1975 as revised in 1983.

### Statistics

All statistics were run by using SAS version 8.1 (SAS Institute, Cary, NC). Analyses of variance were run to determine group differences at 10 wk and at 9 mo postpartum. Additionally, change over time was evaluated with repeated-measures analysis of variance and a Duncan post hoc test; significant covariates were entered into the model statement if necessary to control for nonrandom distributions of baseline variables. These covariates included items such as age, education level, family income, number of individuals living in the household, and presence or absence of the father in the home. Comparisons were considered significant at the  $P < 0.05$  level. Analyses at baseline for group differences were analyzed both with and without the inclusion of subjects who later failed to return to the clinic for the final evaluation.

## RESULTS

Of the 106 women identified as potential subjects, 95 were enrolled in the study. Of the 95 women who participated at baseline, mother-child interactions were recorded and scored for 80 of these dyads. At endpoint, 81 women returned to finish the study and mother-child interaction was recorded and scored for



**FIGURE 1.** Flow diagram of mothers involved in the study and of the analyses. Control mothers (CN) were matched for age, parity, and level of maternal education to the iron-deficient–anemic mothers given iron supplements (IDA-Fe) and to the iron-deficient–anemic mothers given placebo (IDA-PL).

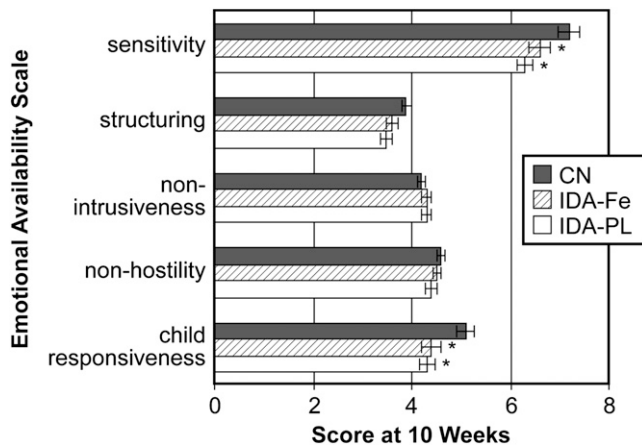
66 of these dyads (**Figure 1**). These 66 women did not differ from others within their respective groups with respect to hematologic, cognitive, or behavioral characteristics (11, 12). Fourteen dyads did not complete all aspects of the videotaping protocol, Griffith developmental assessment, blood sampling, or cognitive testing; therefore, their data were not included in the final analysis of mother–child interactions. The iron intervention resulted in an improvement in iron status in the anemic women who received iron, but there was no improvement in the iron status of anemic mothers who received the placebo (11). Anemic mothers had an average hemoglobin concentration of  $108 \pm 8$  g/L at 10 wk postpartum, which improved to  $129 \pm 9$  g/L in the group that received iron but to only  $120 \pm 8$  g/L in the placebo group. Serum ferritin improved in the iron treatment group from 11 to 34  $\mu$ g/L, but from only 12 to 17  $\mu$ g/L in the placebo group. None of the mothers in the control group were anemic (hemoglobin of  $\approx 136$  g/L and ferritin of 50  $\mu$ g/L at 10 wk postpartum), and both indexes of iron status remained stable for the duration of the trial.

We used the EAS to rescore the mother–child interactions. At baseline, scores on the scales did not differ between the 2 IDA-PL and IDA-Fe groups. In contrast, the control group scored significantly higher on the sensitivity ( $P = 0.028$ ) and child responsiveness scales ( $P = 0.009$ ) than did the IDA groups (**Figure 2**). At endpoint, the control and IDA-Fe groups no longer differed on any of the scales. The mothers in these 2 groups scored significantly higher than did the mothers in the IDA-PL group on the maternal sensitivity ( $P = 0.032$ ), structuring ( $P = 0.026$ ), and nonhostility ( $P = 0.007$ ) scales (**Figure 3**). The children in the control and IDA-Fe groups scored signifi-

cantly higher on the child responsiveness scale than did the children in the IDA-PL group ( $P = 0.027$ ; **Figure 3**). Repeated-measures analyses of variance showed a significant decrease in scores on the maternal sensitivity, structuring, and nonhostility scales for the IDA-PL and the control groups over time. In contrast, scores for the IDA-Fe group did not change over time, with the exception of a decrease in the nonhostility score (**Figure 3**).

## DISCUSSION

This study makes several important contributions. In poor women, maternal iron deficiency anemia is related to less optimal mother–child interactions, such that the mothers are less emotionally available to their infants and, in turn, the infants are less responsive to their mothers. These alterations in mother–child interactions are responsive to iron therapy. Differences were observed in more variables at the 9-mo time point than at the 10-wk time point. This may be a result of an expanding repertoire of interactions between the mothers and infants at the older age. It may also indicate that the effects of iron deficiency anemia are cumulative, such that they become more evident over time. In fact, our results indicate that providing iron to the IDA-Fe group served a protective function on the basis of the decline in mother–child interaction scores that were observed in the IDA-PL group over time. Although we normally consider that women improve their iron status over a 2–6 mo period postpartum, these data suggest that, in the absence of iron intervention, the improvement in iron status is neither rapid enough nor of sufficient magnitude to prevent behavioral alterations. The readjustment in maternal blood volume and changes in absorption of iron should return



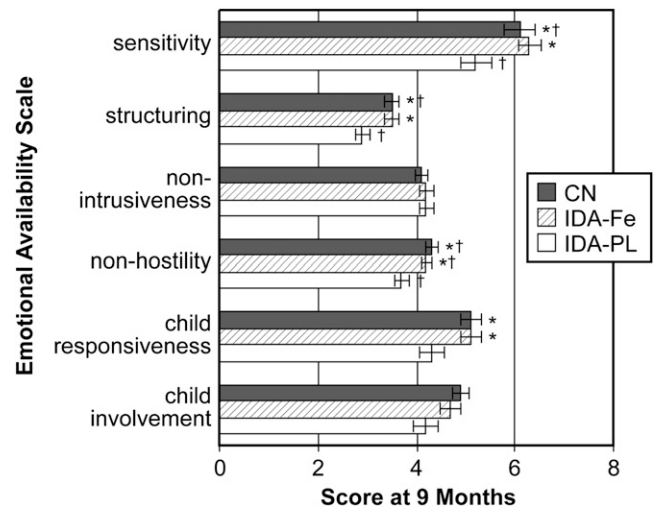
**FIGURE 2.** Mean ( $\pm$ SD) scores on the Emotional Availability Scale at 10 wk postpartum for control women (CN;  $n = 28$ ), iron-deficient-anemic women given iron supplements (IDA-Fe;  $n = 29$ ), and iron-deficient-anemic women given placebo (IDA-PL;  $n = 23$ ). \*Significantly different from the CN group (ANOVA):  $P < 0.03$  (for sensitivity) and  $P < 0.01$  (for responsiveness).

maternal iron status within several months if there is adequate dietary iron available. The current study cannot discern between an immediate benefit within the first several months and a cumulative benefit over the more extended period of the study. Mothers in the control group had a significant decline in sensitivity to their infants at 9 mo compared with their score at 10 wk, which may have been related to the increase in depression experienced by those same mothers (12).

No other studies provide a direct comparison with our current study, but the obvious comparison is with a previous study of mother-child interactions that used a less precise coding system than used in this report—the parent child inventory scale (PCIS) (12). The PCIS focuses on the affective status of the mother and her responsiveness to the infant's needs and initiations. Anemic mothers had more negative statements, less goal setting, and less responsiveness than did control mothers. The current analysis, which used the EAS, provided novel insights because of the greater specificity of coding for infant mannerisms.

As is frequently the case with mothers in the developing world, the mothers in the present study lived under difficult circumstances with a significant amount of anxiety and depression. Thus, a clear causal model relating only iron deficiency to the maternal functioning and mother child interactions is impossible. Corapci et al (14) examined mother-child interactions in 5-y-old children who had either iron deficiency or good iron status in infancy. They report that reciprocity between mother and child and maternal responsiveness was lower in the group that experienced iron deficiency for a prolonged period in infancy than in the group that had good iron status in infancy. Whereas they do not report on the iron status of the mothers in their groups, the alterations they observed in mother-child interactions are similar to those that we observed in our present study. Thus, the interaction between mother and infant is likely affected by the iron nutritional status of both the mother and infant. In the present study, we could not distinguish between the effects of the 2 because infant iron status was not measured.

Alterations in mother-child interactions are especially concerning given the knowledge that mother-child interactions can



**FIGURE 3.** Mean ( $\pm$ SD) scores on the Emotional Availability Scale at 9 mo postpartum for control women (CN;  $n = 22$ ), iron-deficient-anemic women given iron (IDA-Fe;  $n = 25$ ), and iron-deficient-anemic women given placebo (IDA-PL;  $n = 19$ ). \*Significantly different from the IDA-PL group,  $P < 0.03$  (ANOVA). †Significantly different from baseline,  $P < 0.05$ .

influence child development (15). High-quality mother-infant interactions form the basis of a healthy attachment (16), and, during infancy, mothers play a critical role in this interaction. Infants become attached to those associated with consistent, predictable, and appropriate responses to their signals and needs. The IDA mothers in the current study had higher levels of depression and anxiety, but there is no direct evidence that they are more unpredictable (11). Mother-infant interactions are dynamic, well-structured, and nonlinear collaborations. Therefore, a mother's ability to recognize and respond appropriately to her infant's cues are central to healthy mother-child interactions and are related to advances in socioemotional and cognitive domains of child growth (17). Whereas mothers play a critical role in the quality of the mother-infant interaction, infants also influence the interaction. Infants shape and are shaped by the experiences with parents in a reciprocal manner. Some reports indicate that iron-deficient children elicit responses different from those of adults and have alterations in behavior (18). At 4–5 y of age, iron-deficient children had less positive affect and verbalizations and moved closer to their mothers more quickly in a novel situation compared with nonanemic children. The negative feedback loop between less-interacting children and less-responsive adults likely contributes to a sustained pattern of poor emotional development.

In conclusion, this reexamination of mother-child interactions in a group of iron-sufficient and IDA mothers showed that both maternal and infant functioning is altered. Whereas a causal model is not possible regarding which came first, it is nonetheless clear that iron supplementation in the anemic mothers improved their emotional availability. This reexamination of mother-child interactions with a more sensitive scale to assess maternal emotional functioning showed that the sensitivity and responsivity of mothers is strongly affected by iron nutritional status. Future studies should carefully consider maternal nutritional status while evaluating the neurologic growth and development of their infants. (Other articles in this supplement to the Journal include references 19–24.)



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The authors' responsibilities were as follows—LEM-K and JLB: wrote the manuscript; JLB: designed the study; and LEM-K: collected and analyzed the data. Neither author had a personal or financial conflict of interest.

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