The positive effect of low dose iron and zinc intake on child micronutrient status and development during the first 1000 days of life: A systematic review and meta-analysis


Problem at hand
Iron and zinc deficiencies are among the most widespread micronutrient deficiencies. Children and women of all ages are at risk of experiencing concurrent deficiencies, especially in low-income countries. Even mild deficiencies of one or both nutrients may contribute to increased morbidity and mortality. Maternal zinc deficiency could lead to growth retardation and other developmental defects of the foetus while infants iron deficiency (ID) could lead to impairment in their cognitive development and physical performance. Adequate supply of micronutrients during the first 1000 days is essential for normal development and healthy life.

Objectives
The objective of this systemic review and meta-analysis is to assess the potential of interventions delivering iron or zinc in doses up to the RNI levels, from conception to age 2 years, on nutritional status & development.

Materials and methods

Literature Search - A literature search to identify systematic reviews and meta-analyses that investigated the effect of iron and zinc interventions (fortification supplementation) on nutritional, developmental and health outcomes of children was conducted on WHO e-Library of Evidence for Nutrition Actions, the Cochrane Central library, Web of Science, and MEDLINE/PUBMED databases. The search was restricted for studies published between 2005 and 2015.

Out of 4542 relevant searches, 90 publications were selected for inclusion in the final analysis.

Outcome Measures - Outcomes evaluated were: (1) Hb concentration (g/dL); (2) anaemia (%; defined as Hb<110 g/L); (3) serum ferritin concentration (µg/L); (4) ID (%; defined as serum ferritin <10 µg/L or <12 µg/L); (5) IDA (%; defined as Hb<105 g/L or <110 g/L and serum ferritin <10 µg/L or <12 µg/L); (6) serum or plasma zinc (µmol/L); (7) zinc deficiency (%; defined as serum zinc <10.7 µmol/L); (8) birth outcomes (birth weight in g; prevalence of low birth weight in %, defined as weight <2500 g); (9) infant anthropometric measures (height for age z-score (HAZ); weight for age z-score (WAZ); weight for height z-score (WHZ); stunting (≤−2 HAZ scores), wasting (≤−2 WHZ scores) underweight (≤−2 WAZ scores)); (10) mental and motor development [Bayley mental development index (MDI); Bayley psychomotor development index (PDI)]; (11) morbidity (diarrhoea, fever and respiratory infection).

Results
Iron interventions in children 6–23 months of age

Effect on Hb concentration: The effect of up to 15 mg of additional iron daily led to significantly higher Hb concentrations in children, compared with no iron (pooled mean difference 4.07 g/L (95% CI: 2.82, 5.33)).
- **Effect on anaemia prevalence**: The iron interventions delivering 6–8 mg and >8–10 mg iron per day reduce the risk of anaemia by 46% and 41%, respectively.

- **Effect on serum ferritin**: The effect of low dose iron interventions in significantly higher serum ferritin concentrations compared with controls (mean difference 17.3 g/L (95% CI: 13.1, 21.2)).

- **Effect on prevalence of ID and IDA**: Children 6–23 months old with up to 15 mg of iron daily significantly reduced their risk of ID and IDA by 78% (95% CI: 65% to 86% reduction) and 80% (95% CI: 63% to 89% reduction) respectively.

- **Effect on growth and development**: There was no effect of iron on the risk for stunting or wasting. None of the studies reported a beneficial effect of iron on any of the diarrhoea, fever and respiratory infection morbidities also had no effect on mental development and psychomotor development scores.

**Zinc interventions in children 6–23 months of age**

- **Effect on serum or plasma zinc concentrations and zinc deficiency**: Daily zinc administration ≤10 mg suggests that the zinc interventions significantly increased serum or plasma zinc concentrations by 2.03 mol/L compared with no zinc (95% CI 1.21, 2.85 mol/L; p < 0.0001).

- **Effect on growth**: After pooling the studies, Daily zinc administration ≤10 mg interventions compared with no zinc slightly but significantly increased WAZ (mean difference: 0.05, 95% CI 0.0, 0.1) and WHZ (mean difference: 0.04, 95% CI 0.0, 0.08), while the HAZ result was not significant (mean difference: 0.00, 95% CI -0.04, 0.03).

- **Effects on diarrhoea, fever, and respiratory infections**: Of the 16 studies, only 3 found a positive effect of zinc intake.

**Conclusion**

The use of iron in dietary doses (no more than 15 mg/day) during infancy and early childhood had positive effects on hemoglobin levels, anemia prevalence, and iron status (serum ferritin, ID and IDA prevalence).

When zinc and iron were given together, their beneficial effects on serum zinc and iron levels were weaker than when each nutrient was given alone, suggesting that iron and zinc compete for absorption from the gut.

Sub-group analyses demonstrated that iron administered as forticants significantly increased serum ferritin and hemoglobin levels, although to a lesser extent than supplements. This could be due to the presence of absorption inhibitors in fortified foods.

Providing dietary or relatively low daily doses of iron and zinc to young children could be beneficial for their iron and zinc status. Food based approaches are useful tools to reduce the prevalence of iron and zinc deficiencies among infants and young children.
**Problem at hand**

Success of iron and zinc supplementation programmes has been limited due to poor compliance, inadequate programme support and coverage. In India and other developing countries, almost 75% of children suffer from iron deficiency anaemia (IDA) and over 50% have zinc deficiency. Feasible and easily acceptable strategies for delivering iron and zinc in infants and young children needs to be identified.

Recent studies have raised concerns about the success of zinc-iron supplementation in children. So, fortified complementary foods and micronutrient powders could have sustained use as means of delivering micronutrients through food medium.

**Objective**

In the present study, authors evaluated compliance with two home-based fortification strategies, fortified complementary food or sprinkle along with education versus only education, for delivering iron and zinc in 6-24 months old children, over a period of 6 months.

**Materials and methods**

A multi-arm randomized study was conducted in 325 children consuming complementary foods in addition to breast feeding. Eligible children were selected from the clusters and randomized in three groups as given in figure 1. The groups were rice-fortified complementary food and nutrition education, sprinkle and nutrition education, or nutrition education alone as control.

**Figure 1. Overview of study design**

12 clusters in Sangam Vihar  
(25 households in each cluster)

Identified 6-24 months old children  
in the selected clusters (n=325)

Random allocation of four clusters to  
each of three groups

Informed consent taken 292 enrolled  
with no severe illness or severe  
acute malnutrition; 33 refused

Sprinkle  
Enrolled=97  
Refusals=30  
Out-migration=5

Fortified complementary food  
Enrolled=101  
Refusals=9  
Out-migration=6

Nutrition education  
Enrolled=94  
Refusals=5  
Out-migration=2

Follow-up for 6 months
Intervention

- Sachets of fortified complementary food or sprinkle were given once daily to children and monthly to the mother, for six months
- Children < 1 year were given 20g sachet; Children > 1 year had 40-g sachet
- Iron and zinc dosage:
  - 20g sachet: 7.9 mg and 6.5 mg
  - 40g sachet: 15.9 mg and 13.0 mg
- Information on compliance and anthropometry was collected twice in a week
- Complete haemogram was estimation at baseline and end of the study

Results

Baseline characteristics of the three groups were similar. Fortified complementary group achieved higher compliance rate than sprinkle based intervention. Results relating to compliance with fortification are presented in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sprinkle (n=7878 child-days)</th>
<th>Fortified complementary food (n=9532 child-days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days fortification offered</td>
<td>5037 (63.9)</td>
<td>7760 (81.4)</td>
</tr>
<tr>
<td>Amount of fortified food eaten daily (All)</td>
<td>4028 (80.6)</td>
<td>6214 (81.9)</td>
</tr>
</tbody>
</table>

Rice-based fortified complementary food resulted in significant improvement of mean haemoglobin (Hb) compared to the control group (Cf 1.29±1.6 g/dL; Ed 0.23±1.3 g/dL; p<0.001). Proportion of children with anaemia reduced by 67% in the fortified complementary food group. Sprinkle fortification did improve the iron status but these changes were not statistically significant (Table 2).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reduction in proportion of children with anaemia (Hb&lt;10 g/dL)</th>
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</thead>
<tbody>
<tr>
<td>Fortified complementary food (n=66)</td>
<td>67 %</td>
</tr>
<tr>
<td>Sprinkle (n=62)</td>
<td>27 %</td>
</tr>
<tr>
<td>Control (n=48)</td>
<td>22 %</td>
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</table>

Conclusion

Lower compliance observed in sprinkle powder compared to fortified complementary food could have been attributed to either change in taste and/or color of the food in which it was added or due to mother forgetting to give the sprinkle powder.

The present study suggests that micronutrient-fortified complementary food and the use of sprinkle could have sustained use and, thus, are suitable delivery mechanisms of iron and zinc in children between 6-24 months.