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Original Article

Iron intake and iron status in breastfed infants during the first year of life

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SUMMARY

Background & aims: Breastfed infants may be at particular risk for iron deficiency because breast milk is low in iron. In a secondary analysis of data from a complementary feeding trial, indicators of iron status were examined, with particular focus on the development of iron status in those infants who were fully breastfed during the first 4 months of life.
Methods: In this retrospective analysis of data from a randomized controlled trial infants were stratified according to their predominant milk diet during the first 4 months of life, a subgroup of breastfed infants (group BM, $n = 53$) were compared with a subgroup of infants fed (iron-fortified) formula (group F, $n = 23$). Dietary iron intake and indicators of iron status were analysed at 4 months of age (during the full milk feeding period), and during the complementary feeding period at 7 and 10 months of age.
Results: Iron intake was low in the BM group, ranging below the Dietary Reference Intakes throughout the complementary feeding period, with the (estimated) bioavailable iron intake only just achieving the reference requirements. At 4 months, iron deficiency (ID, Ferritin <12.0 ng/mL) was observed in 3 infants in the BM group and in 1 infant in the F group; no infant developed iron deficiency anaemia (IDA, ID and Hb <10.5 g/dl). At 7 and at 10 months of age, iron status was adequate in all infants of the F group. In the BM group, at 7 (10) months of age, ID was diagnosed in 10 (11) infants and IDA was found in 2 (1) infants.
Conclusions: Healthy infants, fully breastfed at 4 months of age, demonstrated ID in about 21% and IDA in up to 6% during the second half of infancy while fed according to the paediatric dietary guidelines. This finding supports the recommendation that supplementation with bioavailable iron via complementary foods should be started early (4–6 months of age) in order to prevent iron deficiency during infancy.
Study registration number (www.clinicaltrials.gov): NCT00571948.

1. Introduction

Breastfeeding is widely accepted as the gold standard for the nutrition of infants during the first months of life. Breast milk cannot meet iron requirements at any age; however iron stores at birth adequately provide for iron needs during the first months of life. During the second 6 months of life, in infants fed breast milk, >90% of iron requirements must be met by complementary feeding to decrease the risk of developing iron deficiency (ID) or even iron deficiency anaemia (IDA), which is thought to be associated with adverse outcomes of neurodevelopment.[1,2]

Prior to 2001, the World Health Organization (WHO) recommended that infants be exclusively breastfed for 4–6 months. In 2001, following a systematic review and expert meeting, this advice was changed to recommending exclusive breastfeeding for the first 6 months of life.[3] At the same time it was recognised that exclusive breastfeeding for the first 6 months may confer a risk of marginal iron status in susceptible infants.[4] This statement was based on one trial in a developing country. Whereas the latest WHO recommendation is still largely undisputed for developing countries, the evidence is somewhat weaker for healthy infants in developed countries, especially as some exclusively breastfed infants may be at risk of specific nutritional deficiencies before 6 months of age.[5] As micronutrient deficiencies represent the most generalised form of

Abbreviations: BA, bioavailable; BM, breast milk; CF, complementary food; DINO, Dortmund Intervention Trial for Optimization of Infant Nutrition; DRI, Dietary Reference Intake; F, formula; Fe, serum-iron; Fer, serum-ferritin; Hb, haemoglobin; Hct, haematocrit; HM, high meat; ID, iron deficiency; IDA, iron deficiency anaemia; LM, low meat; MCH, mean cell haemoglobin; MCV, mean cell volume; RBC, red blood cells (Erythrocytes); Ret, reticulocytes; RCT, randomised controlled trial; TEE, total energy expenditure; TfR, soluble transferrin-receptor; ZPP, zinc protoporphyrine.

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malnutrition in the world,[6] with the prevalence of iron deficiency anaemia (IDA) estimated at approximately 42% in developing countries and 17% in developed countries,[7] adequate iron intake through complementary feeding is of particular importance for meeting increasing iron demands during the second half of infancy. German and European paediatric guidelines recommend introducing complementary food (CF) between 17 weeks and 26 weeks of life.[8,9] In spite of growing awareness that nutrition during infancy may have profound biological effects and important consequences for both short- and long-term health, knowledge of the regulation of iron metabolism in healthy breastfed infants during the period of complementary feeding is still limited.[1,5]

The Dortmund Intervention Trial for Optimization of Infant Nutrition (DINO) is a double-blinded, randomized, controlled intervention trial (RCT) that compared the effect of high-meat CF with low meat CF on iron status during infancy.[10] In addition, fatty acid status was examined.[11] In the primary analysis of the RCT data we showed, that the current low meat content of commercial CF did not significantly impair iron status in a group of healthy infants, comprising both breastfed and formula fed infants who were fed according the current paediatric dietary guidelines.[10] However, trends for iron biomarkers were slightly more favourable in the intervention group with the higher level of meat intake. The aim of this secondary analysis of the DINO study data was to examine the development of iron status during infancy in the subgroup of infants who were fully breastfed for at least 4 months.

2. Methods

2.1. Study design and subjects

In the DINO study dietary intake and indicators of iron status were prospectively recorded in a cohort of healthy infants. Mothers and their newborns were recruited in delivery hospitals located in the area of Dortmund, Germany, between September 2005 and July 2006. Inclusion criteria were as follows: term birth >37 weeks, birth weight >2500 g, intention to breastfeed, and intention to feed the complementary intervention diet according to the study protocol.

The intervention in the DINO study examined the effect of consuming complementary food with a ‘low’ meat content (LM: 8% of weight, the lowest permitted level in the European Community (EC) food legislation)[12] versus CF with a ‘high’ meat content (HM: 12% of weight, recommended by the German dietary guidelines). Study food was provided in the form of commercial vegetable–meat-meals in jars (produced by the companies Hipp, Pfaffenhofen, and Nestlé, Frankfurt, Germany). All parents were advised to start complementary feeding by using the study food between the age of 4 and 6 months (weeks 17–26) and to continue until the age of 10 months, with a frequency of one jar per day at least five times per week. For the remaining meals (e.g. breastfeeding, formula, porridge, fruit, bread) the parents were counselled according the Germany paediatric guidelines;[9,13] exact timing and choice of foods were left to the parents.[10]

2.2. Dietary assessment

From the age of two months, parents kept a daily record of type and amount of each food and beverage consumed by their infant, apart from breast milk, and collected product packages to provide detailed information about food composition.

The consumption of breast milk and the respective energy intake (69 kcal/100 mL)[14] was estimated based on the assumption that healthy, normally growing infants self-regulate their energy intake by their total energy expenditure (TEE). Data on TEE were taken from a recent reference.[15] This assumption proved to be valid throughout the first year of life at a group level for healthy infants fully breastfed for at least 4 months.[16]

The mean iron content of fortified formula milk selected by the study participants was 5.6 mg per 100 g powder (0.84 mg/100 mL). The iron content of breast milk was assumed to be 0.058 mg iron per 100 mL.[14] Iron content of CF was analysed in the case of the study food and estimated by recipe simulation based on the labelled ingredients for CF other than study food. The amount of iron assumed to be absorbed (bioavailable (BA) iron) from different kinds of food was estimated by applying food-specific values from the literature: breast milk, 34%;[17] formula, 20%;[18] meat, 15.5%;[19] fruits, 10%; vegetables, 13.5%;[20] cereals, 4%;[21] iron-fortified infant cereals, 3%.[22] In Germany, only CF in the form of milk–cereal meals and some milk-free cereal products are supplemented with iron.

Table 1
Basic characteristics of participants in the groups ‘Breast Milk’ and ‘Formula’ and in the subgroup of breastfed infants diagnosed with iron deficiency (ID, Fer <12 ng/mL) or iron deficiency anaemia (IDA, Fer <12 ng/mL and Hb <10.5 g/dL) at 7 or 10 months.

	Formula ($n = 23$)	Breast Milk ($n = 53$)	p[d]	ID ($n = 14$)	IDA ($n = 3$)	p[e]
Child						
Boys/Girls (n)	8/15	27/26	n.s.[b]	8/6	1/2	n.s.[b]
Gestational age (weeks)[a]	39.6 (1.3)	39.7 (1.1)	n.s.[c]	39.8 (1.2)	39.7 (1.5)	n.s.[c]
Birth weight (kg)[a]	3.3 (0.4)	3.5 (0.4)	n.s.[c]	3.4 (0.4)	3.1 (0.4)	n.s.[c]
Bodyweight at 4 mo (kg)[a]	6.8 (0.5)	6.9 (0.8)	n.s.[c]	7.2 (0.8)	6.9 (1.5)	n.s.[c]
Bodyweight at 7 mo (kg)[a]	8.3 (0.7)	8.2 (0.8)	n.s.[c]	8.3 (0.8)	8.1 (1.4)	n.s.[c]
Bodyweight at 10 mo (kg)[a]	9.1 (0.9)	9.0 (0.9)	n.s.[c]	9.2 (0.8)	9.0 (1.3)	n.s.[c]
Start of Complementary feeding (weeks)[a]	19 (3.5)	23 (2.9)	**<0.001**[c]	24 (2.7)	25 (3.1)	n.s.[c]
Mother						
Age (years)	32	34	n.s.[c]	35	39	n.s.[c]
Primipara (%)	65	59	n.s.[b]	57	67	n.s.[b]
University entrance diploma (%)	44	83	**<0.05**[a]	100	100	n.s.[a]
Smoking during pregnancy (%)	26	6	**<0.05**[b]	7	0	n.s.[b]
Iron supplement during pregnancy (%)	52	49	n.s.[b]	43	33	n.s.[b]

[a] Mean (SD).
[b] χ^2.
[c] Wilcoxon-two-sample-test.
[d] Comparison of group Breast Milk to group Formula.
[e] Comparison of subgroup ID ($n = 14$) to breastfed infants without ID ($n = 39$).

Table 2
Mean (95% Confidence Interval) of daily intake of iron and iron assumed to be absorbed (BA iron) during **months 3–10** in the groups 'Breast Milk' and 'Formula' and in the subgroup of breastfed infants diagnosed with iron deficiency (ID Fer <12 ng/mL) or iron deficiency anaemia (IDA. Fer <12 ng/mL and Hb <10.5 g/dL) at 7 or 10 months.

	Formula ($n = 23$)	Breast Milk ($n = 53$)	p[a]	ID ($n = 14$)	IDA ($n = 3$)	p[a,b]
Months 3–4						
Iron (mg/d)	6.14 (5.43; 6.86)	0.46 (0.44; 0.47)	<0.0001	0.46 (0.43; 0.44)	0.44 (0.23; 0.65)	n.s.
% from Milk or Formula	99.3%	98.4%		100%	100%	
BA iron (mg/d)	1.22 (1.08; 1.36)	0.15 (0.15; 0.16)	<0.0001	0.16 (0.15; 0.17)	0.15 (0.08; 0.22)	n.s.
% from Milk or Formula	99.8%	98.6%		100%	100%	
Months 5–7						
Iron (mg/d)	6.99 (6.41; 7.57)	1.55 (1.29; 1.81)	<0.0001	1.17 (0.83; 1.52)	0.68 (0.38; 0.97)	n.s.
% from Milk or Formula	77.9%	45.1%		57.9%	86.4%	
% from MCM	12.3%	20.5%		18.0%	6.9%	
BA iron (mg/d)	1.20 (1.06; 1.33)	0.27 (0.24; 0.30)	<0.0001	0.23 (0.21; 0.24)	0.20 (0.13; 0.28)	n.s.
% from Milk or Formula	90.0%	69.1%		81.9%	96.8%	
% from MCM	3.6%	6.3%		4.9%	1.1%	
Months 8–10						
Iron (mg/d)	6.96 (6.39; 7.52)	4.81 (4.29; 5.34)	<0.0001	4.63 (3.17; 6.09)	1.88 (0.11; 3.65)	n.s.
% from Milk or Formula	45.2%	7.5%		12.1%	32.3%	
% from MCM	33.7%	30.4%		27.6%	28.9%	
BA iron (mg/d)	0.88 (0.72; 1.03)	0.58 (0.51; 0.66)	0.0011	0.54 (0.39; 0.68)	0.28 (0.18; 0.37)	n.s.
% from Milk or Formula	66.4%	19.6%		26.7%	66.5%	
% from MCM	14.4%	12.8%		11.8%	8.9%	

Milk = breast milk in group Breast Milk (BM), ID and IDA, and Formula in group Formula (F).
[a] Wilcoxon-two-sample test; Iron = calculated; BA = estimated from food-specific bioavailability values.
[b] Comparison of the group ID ($n = 14$) to the subgroup of breastfed infants without ID ($n = 39$); MCM, milk–cereal meal.

2.3. Study groups

No infant received complementary food during the first 4 months of life. For this data analysis, infants who provided complete data for all variables considered here were retrospectively stratified into three groups according to their predominant milk diet during the first 4 months. Infants ($n = 53$) were assigned to the breast milk (BM) group if they received >95% of energy from breast milk during months 3 and 4, and to the formula (F) group ($n = 23$) if they received >95% of energy from formula. Infants who received both breast milk and formula during months 3 and 4 ($n = 18$) were not analysed further here.

2.4. Clinical assessment

Infants were medically examined at the Children's Hospital in Dortmund at the age of 4 months (129 ± 5 days), 7 months (221 ± 6 days) and 10 months (310 ± 5 days). Weight, length, and head circumference were measured and parents were interviewed about recent illness, febrile infections and other medical complications. Non-fasting venous blood samples were obtained and were analysed for 14 indicators. Here we report on 10 indicators of iron status: haemoglobin (Hb), haematocrit (Hct), mean cell volume (MCV), mean cell haemoglobin (MCH), red blood cells (RBC), reticulocytes (Ret), serum-ferritin (Fer, Luminescence-Immuno-Assay (LIA)), soluble transferrin-receptor (TfR, nephelometric determination (using BN-ProSpect, Dade Behring, Marburg, Germany)), zinc-protoporphyrine (ZPP) and serum-iron (Fe). For the present analysis, we defined iron deficiency (ID) as a serum-ferritin value below 12 ng/mL (indicating exhausted iron stores) and iron deficiency anaemia (IDA) as ID and additional Hb below 10.5 g/dL.[23]

2.5. Statistical methods

Statistical analyses were performed using SAS® (SAS Inc., Cary, NC, USA), software versions 8e and 9.1 for Windows®. For comparison of groups the procedure FREQ (PROC FREQ) was used, including the χ^2-test and the Wilcoxon-two-sample test (PROC NPAR1WAY). For analyses of variance (ANOVA; PROC GLM) models were adjusted for sex and birth weight and were tested for interaction.

2.6. Ethical considerations

The DINO study was approved by the Ethical Committee of the Faculty of Medicine University of Muenster. Parents gave written informed consent to participate.

3. Results

3.1. Subjects

Infants in the BM and F groups did not differ in terms of basic characteristics, including weight at birth and at 4, 7 and 10 months of age (Table 1). A significantly higher percentage of mothers in the BM group had a high school diploma and a significantly lower percentage smoked during pregnancy in comparison to the mothers in the F group. Random allocation to LM and HM intervention meals resulted in equal proportions in the subgroups (LM/HM: 26/27 in the BM group, and 11/12 in the F group). CF was introduced later in the BM group than in the F group. At 7 and 10 months of age, 89% and 40% of infants, respectively, were still partially breastfed in the BM group (data not shown).

Table 3a
Means (95% Confidence Interval) of selected indicators of iron status in **4 months** old infants in the groups 'Breast Milk' and 'Formula'.

	Breast Milk ($n = 53$)	Formula ($n = 23$)	p[a]
Clinical indicators			
Haemoglobin (g/dl)	11.8 (11.6; 12.0)	12.0 (11.7; 12.4)	0.3393
Haematocrit (%)	35.9 (35.3; 36.5)	35.9 (34.9; 36.9)	0.9791
MCV (fl)	81.1 (80.2; 82.0)	81.6 (80.0; 83.3)	0.3650
MCH (pg)	26.7 (26.4; 27.0)	27.2 (26.7; 27.8)	**0.0410**
RBC (10^6/µl)	4.4 (4.4; 4.5)	4.4 (4.3; 4.6)	0.6411
Reticulocytes (‰)	8.3 (7.7; 8.9)	8.4 (7.2; 9.6)	0.8661
Functional indicators			
Ferritin (ng/mL)	75.2 (59.4; 91.0)	63.4 (45.8; 81.1)	0.3786
TfR (mg/l)	1.7 (1.6; 1.8)	1.6 (1.4; 1.7)	0.0577
ZPP (µmol/mol Heme)	37.1 (32.4; 41.9)	48.6 (37.1; 60.1)	**0.0174**
Iron (µg/dl)	57.4 (52.5; 62.4)	69.7 (59.7; 79.7)	**0.0040**

[a] ANOVA (adjusted for birth weight and sex).

3.2. Iron intake

At 4, 7, and 10 months of age, infants in the BM group had a lower daily iron intake than infants in the F group. The low iron intake of the BM-group infants increased considerably upon introduction of CF (Table 2). Almost all infants received iron-fortified cereal products, which provided about 13% of total iron intake during months 7–10, similarly in the breastfed and formula fed infants.

3.3. Iron status

At 4 months of age, ID was observed in 3/53 (6%) infants of the BM group and in 1/23 (4%) infant of the F group; no infant was observed with IDA, irrespective of the type of milk feeding. In general, indicators did not point to a severely impaired iron metabolism at 4 months of age (Table 3a).

During the complementary feeding period, at 7 and 10 months of age, infants in the BM group presented with lower values for Hb, Hct, MCV, MCH, and iron compared to infants in the F group. Moreover, at 10 months of age, Fer was lower and TfR higher in BM-group infants compared to the F-group infants (Tables 3b and c), indicating nearly exhausted body iron stores and an increasing need for additional iron intake in the breastfed infants.

At 7 months of age, ID was observed in 10/53 (19%) infants in the BM group; 2/53 (4%) infants were diagnosed with IDA. At 10 months of age, ID was observed in 11/53 (21%) infants of the BM group; 1/53 (2%) infant was diagnosed with IDA. 3/53 (6%) further infants in the BM group presented with Hb values between 10.0 and 10.5 at 10 months of age, but without Fer values below 12 ng/mL. We did not find any significant differences between those infants with exhausted iron status parameters and all other infants in the BM group in terms of basic characteristics (Table 1) or estimated intake of iron and BA iron (Table 2).

In contrast, in all infants of the F group, iron status was adequate at 7 and at 10 months of age.

Table 3b
Means (95% Confidence Interval) of selected indicators of iron status in **7 months** old infants in the groups 'Breast Milk' and 'Formula'.

	Breast Milk ($n = 53$)	Formula ($n = 23$)	p[a]
Clinical indicators			
Haemoglobin (g/dl)	11.4 (11.3; 11.6)	12.1 (11.8; 12.5)	**0.0002**
Haematocrit (%)	35.5 (35.0; 35.9)	36.7 (35.8; 37.7)	**0.0113**
MCV (fl)	78.1 (77.1; 79.1)	80.0 (78.3; 81.8)	**0.0259**
MCH (pg)	25.2 (24.9; 25.5)	26.4 (26.0; 26.9)	**<0.0001**
RBC (10^6/µl)	4.6 (4.5; 4.6)	4.6 (4.5; 4.7)	0.6544
Reticulocytes (‰)	8.8 (7.9; 9.6)	8.8 (7.7; 9.9)	0.8697
Functional indicators			
Ferritin (ng/mL)	32.5 (25.5; 39.5)	36.4 (29.7; 43.1)	0.5685
TfR (mg/l)	1.8 (1.7; 2.0)	1.7 (1.6; 1.8)	**0.0169**
ZPP (µmol/mol Heme)	38.8 (32.8; 44.8)	40.8 (34.4; 47.2)	0.8243
Iron (µg/dl)	53.5 (48.2; 58.9)	66.1 (55.2; 77.0)	**0.0122**

[a] ANOVA (adjusted for birth weight and sex).

4. Discussion

In our study group of healthy infants, 6% of those who had been fully breastfed for 4 months as per current dietary guidelines presented with iron deficiency, none of these though with anaemia at the age of 4 months. The low dietary iron intake in these infants only increased slowly with the introduction of non-iron-fortified, but meat-containing CF. During the complementary feeding period, indicators of iron metabolism pointed to activation of mechanisms that increase the efficacy of iron metabolism. At 7 and 10 months of age about 21% of formerly fully breastfed infants were diagnosed with ID and 6% with manifest IDA. These data imply that otherwise healthy, but susceptible infants may be at a considerable risk of developing iron deficiency if they are exclusively breastfed for longer than 4 months.

4.1. Infant characteristics

All infants participating in the DINO study were healthy, born at full term, with normal weights and well nourished. Due to observations linking birth weight and postnatal weight gain to lower levels of indicators of iron status, all models in our analyses were adjusted for birth weight. Furthermore, there were no differences in weight at 4, 7, and 10 months of age between the milk subgroups. Some confounding factors, such as educational level or smoking during pregnancy of the mother may influence the decision to breastfeed. Unfortunately, we did not measure Hb at birth; however, at 4 months of age, Hb levels did not differ between the BM and the FM group as might have been expected.[24–26]

4.2. Iron status and iron intake

Despite the longstanding debate about the optimal duration of exclusive breastfeeding, very few studies with detailed dietary data and long-term observation of iron status in breastfed infants have been published.[27,28] In addition, there is an ongoing discussion as to the exact definition of IDA in infants.[29] With regards to clinical relevance, Hb is the most interesting indicator, as it reflects the overall effect of iron metabolism on erythropoesis. Whereas most

Table 3c
Means (95% Confidence Interval) of selected indicators of iron status in **10 months** old infants in the groups 'Breast Milk' and 'Formula'.

	Breast Milk ($n = 53$)	Formula ($n = 23$)	p[a]
Clinical indicators			
Haemoglobin (g/dl)	11.9 (11.6; 12.1)	12.3 (12.0; 12.7)	**0.0285**
Haematocrit (%)	36.3 (35.7; 37.0)	37.5 (36.6; 38.4)	**0.0463**
MCV (fl)	77.8 (76.9; 78.7)	79.8 (78.5; 81.2)	**0.0022**
MCH (pg)	25.2 (24.9; 25.6)	26.3 (25.8; 26.7)	**0.0007**
RBC (10^6/µl)	4.7 (4.6; 4.8)	4.7 (4.6; 4.8)	0.7155
Reticulocytes (‰)	7.8 (7.1; 8.5)	8.1 (6.7; 9.6)	0.8969
Functional indicators			
Ferritin (ng/mL)	23.5 (19.6; 27.4)	35.6 (27.2; 43.9)	**0.0106**
TfR (mg/l)	1.9 (1.7; 2.0)	1.6 (1.5; 1.8)	**0.0228**
ZPP (µmol/mol Heme)	48.4 (41.7; 55.2)	47.2 (39.8; 54.6)	0.6466
Iron (µg/dl)	54.7 (48.4; 61.0)	76.5 (50.4; 102.6)	0.0878

[a] ANOVA (adjusted for birth weight and sex).

iron is bound in RBCs, Fer indicates iron stores in the liver, spleen and in bone marrow.[30] TfR and ZPP are functional indicators of iron status and their increase is attributed to iron deficiency or higher iron requirements.[31]

The results from our study regarding iron status at 4 months of age indicated that some fully breastfed infants may develop iron deficiency. However, at 4 months of age, none of the breastfed infants was observed with iron deficiency anaemia and their iron status was no worse than that of infants fed iron-fortified cow's milk-based formula, although formula contained about the ten-fold amount of iron than breast milk does (0.84 mg/100 mL vs. 0.058 mg/100 mL).

International panels estimate the total iron requirement of 7–12 months old infants at about 0.7 mg/d (as absorbed amount), equivalent to 8 or 11 mg/d dietary iron respectively, when considering the absorption.[32,33] It seems that no benefit can be expected from repletion of iron stores beyond the physiological requirements.[34] Moreover, there is some indication that higher levels of iron in formula may be harmful to infant development.[35]

Several studies have generally shown an inverse correlation between duration of breastfeeding and iron status.[24–26] In our sample, the total amount of dietary iron and estimated BA iron was still low in breastfed infants despite introduction of CF, and only increased slowly with the introduction of meat, and later iron-fortified, cereal-based meals. The increased need for dietary iron in the BM group was reflected in lower Hb values and in functional indicators of iron status pointing to the exhaustion of body stores at 7 and 10 months of age. The slight but continuous increase of TfR from 4 to 10 months of age may reflect the need to utilise iron effectively under conditions of low dietary intake and decreasing body stores. However, mean values of neither TfR nor ZPP reached levels high enough to indicate manifest iron deficiency in our group of BM infants.[36–38]

All in all, these observations may indicate the activation of mechanisms to optimise efficacy of iron metabolism under conditions of increasing iron demand but still relatively low dietary iron intake.[39] Up to 6% of infants that were fully breastfed for 4 months developed iron deficiency anaemia later in infancy, thus supporting the recommending firstly the selection of CF with highly bioavailable iron,[40–42] and secondly the timely introduction of CF in healthy, breastfed infants in developed countries.[5,43]

5. Conclusion

This retrospective analysis of data from the randomised, controlled DINO study supports the hypothesis that a healthy breastfed baby is protected against manifest iron deficiency anaemia during the first months of life, although some susceptible infants may develop iron deficiency. The finding of iron deficiency anaemia in 6% of formerly breastfed infants at 7 or 10 months of age who had been fully breastfed for the first 4 months of life supports the recommendation of a timely introduction of iron-rich CF in breastfed infants in developed countries. Some healthy, full-term breastfed infants may otherwise be susceptible to iron deficiency, and additionally even to iron deficiency anaemia due to the late introduction of CF, even when readily bioavailable iron via CF is provided and total iron intake increases considerably during the second half of infancy. However, further prospective trials are necessary in order to study this question more thoroughly.

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Author's statement

All authors have made substantial contributions and final approval of the conceptions, drafting, and final version of this manuscript.

The authors' responsibilities were as follows – MK and HK: design of the study; KD and JS: conduction of the study and data collection; KD: draft of the manuscript, statistical analysis; MK, HK and MJM: supervision.

Conflict of interest

All authors have no conflict of interest.

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