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Iron deficiency anemia in infants in Sousa (PB), Brazil: an association with nutritional status

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SUMMARY

OBJECTIVE: The aim of this study was to describe the prevalence of anemia and iron deficiency anemia (IDA) in infants and verify the association of iron deficiency with nutritional status.

METHODS: This cross-sectional and observational study included 104 infants aged between 7 and 9 months, assisted from August to September 2021 by the Family Health Strategy program in Sousa municipality (Paraíba, Brazil). Clinical and anthropometric data were collected, and a 24-h food recall questionnaire was applied using the DietPro software (version 5.0) in order to verify food consumption and assess iron intake. Variables associated with iron deficiency ($p<0.05$) were analyzed using multiple logistic regression.

RESULTS: Anemia and IDA were observed in 40.4% and 19.2% of infants, respectively. Only one infant was taking prophylactic supplementation (ferrous sulfate). Infants with IDA presented reduced hemoglobin ($p<0.001$) and ferritin ($p<0.001$) and increased Z-scores of body mass index-for-age (Z-BMI) ($p=0.027$), weight-for-height ($p=0.007$), and weight-for-age ($p=0.032$). All Z-scores were inversely correlated with ferritin (Z-BMI [rho: -0.37; $p<0.001$], weight-for-height [rho: -0.37; $p<0.001$], and weight-for-age [rho: -0.29; $p=0.002$]). Ferritin was also directly correlated with daily iron intake (rho: 0.22; $p=0.018$). Finally, multiple logistic regression showed a significant and direct association of iron deficiency with weight-for-height Z-score (odds ratio: 2.86; 95% confidence interval: 1.38–5.64; $p=0.004$).

CONCLUSION: About 60% of infants presented anemia or IDA. Iron deficiency was associated with the weight-for-height Z-score, showing the vulnerability of infants during the introduction of complementary feeding.

KEYWORDS: Anemia. Iron deficiency anemia. Nutritional status. Infant. Iron.

INTRODUCTION

During the introduction of complementary feeding, infants are vulnerable to micronutrient deficiency, including iron deficiency (ID)[1]. According to the World Health Organization (WHO), 42% of children aged between 6 and 59 months have anemia[2]. In Brazil, 18.9% of infants aged between 6 and 23 months have anemia[3].

Iron deficiency anemia (IDA) is a major contributor to the global burden of disease, affecting especially children in underdeveloped and developing countries[4]. Iron is an essential micronutrient for several functions, especially growth and development, and ID may result in irreversible deficits in cognition, motor function, and behavior[5].

Prophylactic supplementation with ferrous sulfate has a good cost-effectiveness ratio for preventing anemia and ID with the stimulation and promotion of breastfeeding and timely and healthy complementary feeding. This supplementation has been encouraged in Brazil since 2005, for which the Brazilian Society of Pediatrics (SBP) recommends oral intake for healthy and exclusively breastfed infants starting at 6 months[6,7]. Regarding risk factors for ID, SBP recommends anticipating the supplementation[8].

Despite the widely described control strategies, anemia is still prevalent in Brazilian infants, especially in the northeast region. In this sense, studying predisposing factors for ID could ensure a better approach to the disease. Therefore, this study aimed to describe the prevalence of anemia and IDA in infants and verify the association of ID with nutritional status.

METHODS

This observational and cross-sectional study included 104 infants aged between 7 and 9 months from Sousa municipality (Paraíba, Brazil). The study was approved by the research ethics committee of the *Centro Universitário FMABC* (number 3.436.978).

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Sousa municipality has an estimated population of 69,997 people, a human development index of 0.668, and 100% Family Health Strategy coverage.

Infants were recruited in July 2021, and clinical and laboratory data were collected from August to September 2021. During this period, 234 infants (7–9 months) were identified. This age group was selected based on the high vulnerability to anemia during the introduction of complementary feeding. The Family Health Strategy attended 137 infants, and 104 caregivers agreed to participate in the study (Figure 1).

Preterm infants, twins, those with chronic diseases, and those presenting any infection up to 1 month before data collection were excluded.

A questionnaire collected the following data: demographic (gender, birth weight, age, and the number of siblings), caregiver (age and maternal educational level), nutritional status and feeding habits of the infant (duration of exclusive breastfeeding, age of introduction of complementary feeding, and presence of disease), and prophylactic supplementation with ferrous sulfate. A 24-h food recall questionnaire was also applied using the DietPro software (version 5.0) to assess iron intake. The dietary reference and recommended dietary allowance guided the adequacy of iron intake[9]. A single researcher (nutritionist and main investigator) applied the questionnaires.

For anthropometric assessments, Z-scores for height-for-age, weight-for-age, weight-for-height, and body mass index-for-age (Z-BMI; weight divided by the squared height) were obtained by a single nutritionist using the WHO Anthro software[10]. Weight was obtained using a digital scale (infant without clothes or diapers), and height was obtained using a stadiometer (infant in a supine position).

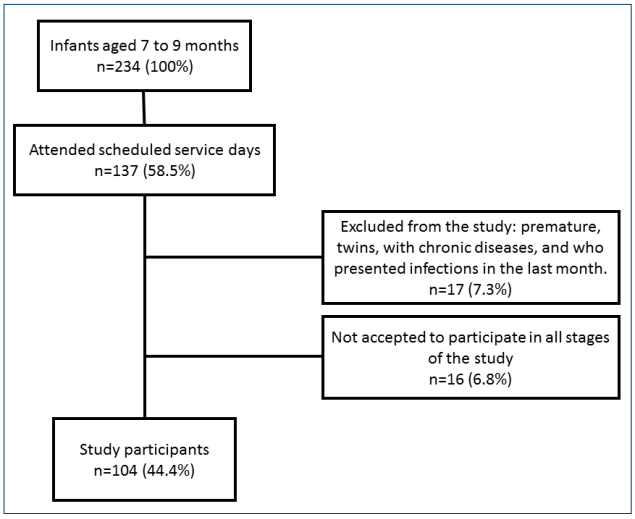

Figure 1. Study flowchart.

Laboratory tests were performed with a 3-h fast 2 days after questionnaires in order to assess anemia and nutritional status of iron. These tests included blood count (automated method), ferritin (chemiluminescence method), serum iron (colorimetric method), and C-reactive protein (CRP; latex agglutination method). CRP was qualitatively classified as normal (≤5 mg/L) or abnormal (>5 mg/L).

Anthropometric and laboratory variables were compared among three groups: without anemia and ID (hemoglobin [Hb] ≥11 g/dL and ferritin ≥12 µg/L if CRP ≤5 mg/L, or ferritin ≥30 µg/L if CRP >5 mg/L), with anemia (Hb <11 g/dL and ferritin ≥12 µg/L if CRP ≤5 mg/L, or ferritin ≥30 µg/L if CRP >5 mg/L)[11], and with IDA (Hb <11 g/dL and ferritin <12 µg/L if CRP ≤5 mg/L, or ferritin <30 µg/L if CRP >5 mg/L)[12]. Serum iron under 30 mg/dL was considered ferropenia[13].

Data were analyzed using the SPSS software version 25.0 (IBM®). The chi-square test compared qualitative variables, and the Spearman's rank correlation coefficient (rho) analyzed correlations between variables. The multiple logistic regressions used a selection template hierarchy for independent variables and considered ID as a dependent variable[14]. Statistical significance was set at 5%.

RESULTS

This study included 104 infants (65.4% female) aged between 7 and 9 months (7.93±0.82 months). We excluded 17 infants (7.3%) who were preterm, twins, presented infection up to 1 month before data collection, and with chronic diseases (Figure 1). Table 1 shows the general characteristics of infants.

Regarding nutritional status, 49% of infants had a Z-BMI over +1 (risk of overweight, overweight, and obesity). Anemia and IDA were observed in 40.4% and 19.2% of infants, respectively. Only one infant took prophylactic supplementation with ferrous sulfate (Table 1).

Table 2 compares general and laboratory data among groups. Infants with IDA presented a higher Z-BMI than infants with anemia or without anemia and ID (p=0.021). Moreover, 90% of infants with IDA presented Z-BMI over +1, increased CRP (p=0.001), and reduced mean corpuscular volume (p<0.001). They also presented increased Z-BMI (p=0.027), weight-for-height Z-score (p=0.007), and weight-for-age Z-score (p=0.032), and reduced Hb (p<0.001) and ferritin (p<0.001) in continuous variables.

Ferritin was directly correlated with iron intake (rho: 0.229; p=0.018) and inversely correlated with Z-BMI (rho: -0.37; p<0.001), weight-for-height (rho: -0.37; p<0.001), and weight-for-age Z-scores (rho: -0.297; p=0.002).

Table 1. General characteristics and laboratory variables of the evaluated infants (n=104).

Variable	n	%
Gender		
Female	68	65.4
Mother's age (years)		
<20	13	12.5
20–30	52	50
30–40	36	34.6
≥40	3	2.9
Maternal education (years)		
0	4	3.9
<4	7	6.7
4–6	38	36.5
6–8	32	30.8
≥8	23	22.1
Attending monthly childcare		
Yes	36	34.6
Received nutritional guidance		
Yes	36	34.6
Infant's age (months)		
7	39	37.5
8	33	31.7
9	32	30.8
Infant's number of siblings		
0	52	50
1	39	37.5
2	11	10.6
3	2	1.9
Birth weight (g)		
≥2,500	103	99
Received exclusive BM up to the 6 months		
Yes	17	16.3
Supplemented BM before 6 months		
Yes	64	61.5
Receiving BM at the moment		
Yes	50	48.1
Receiving powdered milk		
Yes	95	91.4
Receiving cow's milk		
Yes	6	5.8
Receiving beef		
Yes	45	43.3
Receiving pork		
Yes	0	0
Receiving chicken		
Yes	61	58.6
Nutritional status (zBMI)		
Normal weight	53	51
Risk of overweight	31	29.8
Overweight	16	15.4
Obesity	4	3.8
Receiving ferrous sulfate		
Yes	1	1
Hemoglobin (g/dL)		
<11	60	57.7
Mean corpuscular volume (fL)		
<75	14	13.5
Serum iron (µg/dL)		
<40	26	25
Ferritin (µg/L)		
Low	20	19.2
CRP (mg/L)		
>5	10	9.6
Anemia		
–	42	40.4
Iron deficiency anemia		
–	20	19.2

BM: breast milk; zBMI: Z-score body mass index; CRP: C-reactive protein. Low ferritin defined by: <12 µg/L if CRP ≤5 mg/L and <30 µg/L if CRP >5 mg/L.

Multiple logistic regression showed that the weight-for-height Z-score was independently associated with ID in infants (odds ratio [OR]: 2.86; 95% confidence interval [CI] 1.38–5.6; p=0.004). The increase of one weight-for-height Z-score was associated with a 2.86-fold chance of ID (Table 3).

DISCUSSION

The present study showed a high prevalence of anemia and IDA in infants from Souza municipality, which was higher than that observed in the Brazilian National Survey of Food and Child Nutrition (ENANI-2020) with 7,473 children aged between 6 and 59 months. According to ENANI-2020, the prevalence of anemia and IDA in Brazil was 18.9% and 8%, respectively, in infants aged 6–23 months. Our cutoff points for anemia and IDA followed the ENANI-2020 recommendation[3]. In a meta-analysis including 37 Brazilian studies with 17,741 children, the prevalence of anemia in children under 5 years old was an important public health issue, affecting mainly those living in low-income communities and indigenous and quilombola populations[15].

Children with high Z-BMI and growth had reduced iron storage and an increased prevalence of IDA. This result may be due to the low iron absorption and sequestration of reticuloendothelial iron caused by chronic inflammation from adiposity[16]. Also, initial iron storage is depleted during child development, which occurs faster in rapidly growing infants[17]. In a cross-sectional study with 1,607 children aged 1–3 years, increased Z-BMI was associated with low ferritin (OR: -1.51 µg/L; 95%CI -2.23 to -0.76; p<0.0001)[18]. Moreover, in a cohort study with 729 infants from birth to 24 months, weight gain in the second year of life was inversely associated with iron storage in apparently healthy children[19].

Ferritin was directly correlated with daily iron intake in infants. In an Indian cross-sectional study with 217,324 children under 5 years, anemia was associated with low iron intake (OR: 0.110; 95%CI 1.084–1.149; p<0.001)[20]. Measures to reduce IDA due to low iron intake include the promotion of breastfeeding and healthy complementary feeding, as recommended by the dietary guidelines for Brazilian children under 2 years old[7]. Furthermore, the Brazilian Ministry of Health suggests the parallel use of prophylactic supplementation with ferrous sulfate and powdered micronutrients[6].

A controlled Brazilian study compared 462 infants aged 6–8 months receiving powdered micronutrients in complementary feeding with 521 nonsupplemented infants. After 60 days, nonsupplemented infants had a higher prevalence of anemia (23.1% vs. 14.3%; p<0.001) and IDA (10.3% vs. 4.9%;

Table 2. Comparison of clinical-demographic and laboratory variables between groups of infants without anemia and iron deficiency, anemia, and iron deficiency anemia (n=104).

Variable	Without anemia and iron deficiency (n=42)	Anemia (n=42)	Iron deficiency anemia (n=20)	p-value
Categorical variables				
Gender				
Male	11 (26.2%)	17 (40.5%)	8 (40%)	0.331*
Age (months)				
7	18 (42.9%)	14 (33.3%)	7 (35%)	0.787*
8	14 (33.3%)	13 (31%)	6 (30%)	
9	10 (23.8%)	15 (35.7%)	7 (35%)	
Number of siblings				
0	19 (45.2%)	23 (54.8%)	10 (50%)	0.386*
1	19 (45.2%)	12 (28.6%)	8 (40%)	
2	3 (7.1%)	7 (16.7%)	1 (5%)	
3	1 (2.4%)	0	1 (5%)	
Birth weight (g)				
<2,500	0	1 (2.4%)	0	0.475*
Received exclusive breastfeeding until 6 months				
Yes	6 (14.3%)	9 (21.4%)	2 (10%)	0.469*
Supplemented breastfeeding before 6 months				
Yes	28 (66.7%)	24 (57.1%)	12 (60%)	0.660*
Receiving breastfeeding now				
Yes	19 (45.2%)	21 (50%)	10 (50%)	0.893*
Receiving infant formula				
Yes	38 (90.5%)	37 (88.1%)	20 (100%)	0.287*
Receiving whole cow's milk				
Yes	3 (7.1%)	3 (7.1%)	0	0.469*
Receiving meat (beef)				
Yes	18 (42.9%)	17 (40.5%)	10 (50%)	0.777*
Receiving poultry				
Yes	28 (66.7%)	24 (57.1%)	9 (45%)	0.261*
Nutritional status (Z-score of body mass index)				
Normal	20 (47.6%)	27 (64.3%)	6 (30%)	0.021*
Overweight risk	17 (40.5%)	8 (19%)	6 (30%)	
Overweight	3 (7.1%)	7 (16.7%)	6 (30%)	
Obesity	2 (4.8%)	0	2 (10%)	
Mother's age (years)				
<20	7 (16.7%)	5 (11.9%)	1 (5%)	0.289*
20–30	16 (38.1%)	26 (61.9%)	10 (50%)	
30–40	17 (40.5%)	11 (26.2%)	8 (40%)	
≥40	2 (4.8%)	0	1 (5%)	

Continue...

Table 2. Continuation.

Variable	Without anemia and iron deficiency (n=42)	Anemia (n=42)	Iron deficiency anemia (n=20)	p-value
Maternal education (years)				
0	2 (4.8%)	2 (4.8%)	0	0.292*
1–4	6 (14.3%)	1 (2.4%)	0	
4–6	14 (33.3%)	16 (38.1%)	8 (40%)	
6–8	13 (31%)	14 (33.3%)	5 (25%)	
≥8	7 (16.7%)	9 (21.4%)	7 (35%)	
Attending monthly childcare				
Yes	11 (26.2%)	17 (40.5%)	8 (40%)	0.125*
Received nutritional guidance				
Yes	11 (26.2%)	17 (40.5%)	8 (40%)	0.331*
Receiving ferrous sulfate				
Yes	0	1 (2.4%)	0	0.475*
Mean corpuscular volume ≥75 fL				
Yes	42 (100%)	36 (85.7%)	12 (60%)	<0.001*
Serum iron ≥40 µg/dL				
Yes	42 (100%)	23 (54.8%)	13 (65%)	<0.001*
C-reactive protein ≤5 mg/L				
Yes	42 (100%)	38 (90.5%)	14 (70%)	0.001*
Continuous variables				
Age				
Months	7.9±0.8	8±0.8	8±0.83	0.459†
Body mass index				
Z-score	1.1 (1.4)	0.76 (1.6)	1.4 (1.9)	0.027‡
Weight-for-height				
Z-score	1.1±1	0.7±1	1.7±1.2	0.007†
Height-for-age				
Z-score	0.11 (1.5)	-0.66 (1.3)	-0.32 (1.2)	0.297‡
Weight-for-age				
Z-score	0.8±1.2	0.3±1.2	1.1±1.3	0.032†
Hemoglobin				
g/dL	12.2±0.7	10.1±0.5	9.8±0.8	<0.001†
Mean corpuscular volume				
fL	86.4 (2.4)	77.5 (1.1)	80.8 (11.4)	<0.001‡
Serum iron				
µg/L	76.3±23.5	51±23.5	59.3±26.9	<0.001†
Ferritin				
µg/L	22.5 (5.6)	23.1 (39.5)	10.4 (4.7)	<0.001‡
Iron intake				
mg/day	26.6 (18.2)	19 (31.4)	13.1 (17.2)	0.060‡
Protein intake				
g/day	23.8 (26)	23.8 (24.3)	25 (26.1)	0.877‡

Anemia: hemoglobin <11 g/dL with normal ferritin. Iron deficiency anemia: hemoglobin <11 g/dL and ferritin <12 ug/L, if C-reactive protein ≤5 mg/L or <30 µg/L, if C-reactive protein >5 mg/L. Significance level of chi-squared test*, Student's t-test†, and Mann-Whitney test‡.

Table 3. Logistic regression of variables associated with iron deficiency in infants (n=104).

Variables	OR	95%CI	p-value
Gender			
Female	-0.02	0.32–3.60	0.987
Age			
Months	-0.05	0.49–1.95	0.957
Weight-for-height			
Z-score	2.86	1.38–5.6	0.004
Height-for-age			
Z-score	-1.47	0.36–1.15	0.141
Receiving BF now			
Sim	0.72	0.48–4.74	0.472
Receiving meat			
Sim	-0.81	0.20–1.91	0.415
Iron intake			
mg/day	-1.69	0.92–1.00	0.322

Dependent variable: iron deficiency defined as: ferritin <12 µg/L if C-reactive protein ≤5 mg/L or ferritin <30 µg/L if C-reactive protein >5 mg/L. OR: odds ratio; CI: confidence interval; BF: breastfeeding.

p=0.002) than infants receiving powdered micronutrients[21]. In a meta-analysis including 136 studies, iron supplementation for infants was associated with a reduced risk of ID (relative risk: 0.21; 95%CI 0.12–0.39; heterogeneity: 94%; p<0.00001) and IDA (relative risk: 0.14; 95%CI 0.04–0.54; heterogeneity: 88%; p=0.004)[22].

Our study corroborated others suggesting that serum iron was not an isolated biomarker to evaluate iron storage. In a review of 22 guidelines, all of them recommended dosing ferritin to classify ID and IDA. From those, 10 recommended transferrin saturation and none recommended isolated serum iron[23].

CRP increased by 30% in infants with IDA, which we could not explain. CRP is an acute-phase protein used to assess inflammation from different etiologies[24]. ID impairs immune function and increases the risk of infections, especially in infants with IDA, exacerbating the inflammatory process and possibly explaining the association found in the study[25]. Since ferritin also increases during inflammation, the WHO published a guideline in 2020 for dosing CRP with ferritin to evaluate ID and recommended an adjustment in ferritin cutoff points for individuals with CRP over 5 mg/L (infants: <12 µg/L if CRP ≤5 mg/L; <30 µg/L if CRP >5 mg/L)[12]. However, we did not find studies associating ID with CRP in infants.

The sample in this study was carefully selected, excluding infants with acute or chronic diseases (i.e., inflammation). In addition, we used ferritin cutoff points considering the inflammation to identify ID. The main limitation of this study was the assessment of a single Brazilian municipality; thus, the data may not represent the general population. In addition, the cross-sectional design hindered the establishment of a cause-effect relationship.

CONCLUSION

This study observed a high prevalence of anemia and IDA (60%) in infants. Also, ID was associated with an increased weight-for-height Z-score.

Therefore, promoting breastfeeding and a balanced, timely, and healthy complementary feeding with iron-rich foods and guiding a prophylactic supplementation of ferrous sulfate and powdered micronutrients are essential to prevent nutritional disorders.

AUTHORS' CONTRIBUTIONS

LKARA: Conceptualization, Data curation, Investigation, Writing – original draft. **JCPF:** Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft. **ROSS:** Conceptualization, Formal analysis, Investigation, Methodology, Validation, Writing – review & editing.

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