

Isolated and combined risks for anemia in children attending the nurseries of daycare centers

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Abstract

Objective: To identify and quantify isolated and combined risk factors for anemia, providing a comprehensive view of the likelihood of its occurrence.

Methods: Cross-sectional study with 482 children aged 4 to 29 months attending the nurseries of philanthropic and public daycare centers in the city of São Paulo, Brazil, who participated in two surveys (2004 and 2007). Mothers were interviewed, blood was collected using digital puncture, and anthropometry was performed. Anemia was characterized by hemoglobin levels below 11 g/dL. Unconditional logistic regression was adjusted for anemia risk factors. A value of $p \leq 0.05$ indicated statistically significant associations. Post-test odds and likelihood ratios were calculated to define post-test probabilities. Epi-Info™ 2000 and Stata 10.0 software packages were used for statistical analysis.

Results: Prevalence of anemia was 43.6% (95%CI 39.1-48.1). The final logistic model included five categorical variables: mother's age less than 28 years (OR = 1.50; $p = 0.041$), per capita income below half a minimum wage (OR = 1.56; $p = 0.029$), exclusive breastfeeding less than 2 months (OR = 1.71; $p = 0.009$), decrease in weight/age z score from birth to survey (OR = 1.47; $p = 0.050$), and age less than 17 months (OR = 2.44; $p < 0,001$). Post-test probabilities in the associations of isolated and combined risk factors for anemia ranged from 54.5 to 100%.

Conclusions: The probability of anemia progressively increased as the identified risk factors were added. This calculation provides a simple and rapid tool for suspicion of anemia in children both in clinical practice and population screening.

J Pediatr (Rio J). 2009;85(3):209-216: Anemia, infant, child daycare centers, risk factors.

Introduction

Iron deficiency anemia is the most common nutritional deficiency worldwide.¹ Researchers have shown high anemia rates in children, mainly in developing countries. In Brazil, recent studies revealed anemia rates of around 50% in children under 5 years of age, with intensity inversely proportional to age.^{2,3}

Iron deficiency anemia is associated with other morbid conditions, as either a cause or effect of these conditions, such as protein-energy malnutrition and higher rates of respiratory and gastrointestinal infections, consequent to immune system involvement, with impairment of the activity of neutrophils and natural killer cells.⁴ This

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situation contributes to worsening health status and continuing mineral deficiency. Besides, hemoglobin levels below 11g/dL, resulting from iron deficiency, are related to low scores in motor activity and mental development tests in children under 5 years of age, which may lead to irreversible behavioral sequelae even after appropriate treatment.^{5,6}

Understanding anemia risk factors has helped the health professional early identify groups that are more vulnerable to this morbidity, indicating priorities in prevention and control action plans and in the allocation of available resources to improve child health care and promotion.

However, the literature provides results that identify individualized risks of infant anemia, but do not offer the health professional, especially the pediatrician, enough information to approach diagnostic probabilities of this specific nutritional deficiency when such factors occur concomitantly in clinical history and examination.

The objective of this study is to identify and quantify isolated and combined risk factors for anemia in infants and, consequently, to provide a comprehensive view of the likelihood of its occurrence in the presence of one or more risk situations.

Methods

The present study uses data from two surveys with infant populations attending public and philanthropic daycare centers in the city of São Paulo, Brazil, in 2004 and 2007, which used the same sampling and data collection procedures.⁷

Survey I was developed from 54 daycare centers located in the central region of the city of São Paulo, Brazil, and survey II from 36 daycare centers of the Education Coordinating Board of the city of Santo Amaro, state of São Paulo, Brazil. In the first stage of sample selection, in both surveys, daycare centers were contacted by telephone and personal visit. Daycare centers which had previously participated in a health survey, did not have a nursery or refused to participate in this project were excluded, resulting in 13 and 18 daycare centers in surveys I and II, respectively.

In the second stage, daycare centers were classified according to priority criteria.⁸ The following criteria were prioritized in descending order of value: larger number of children, larger number of educators, safety of researchers, available transportation and easy access to the center's facilities, and employment of admission rules that ensure service only to low-income families. Based on this methodology, we selected the five and eight public and philanthropic daycare centers best ranked at surveys I and II, respectively.

The initial population of this study comprised 498 children, aged 4 to 29 months, who attended the nurseries of

the 13 selected daycare centers on a regular basis. Exclusions were as follows: five children who presented acute diseases at the time of the surveys; four children who were absent at open-field activities; five children with chronic diseases (two with Down's syndrome, two with cerebral palsy and one with unknown genetic syndrome) and two children whose parents/guardians did not agree to participate in the survey. Other 13 children were excluded only from the multivariate analysis due to absence of data on the selected variables to compose the final logistic model. Therefore, a total of 482 children were selected and studied in the bivariate analysis and 469 children in the multivariate analysis, amounting to a sample loss of 3.2 and 5.8%, respectively.

A structured and pre-encoded questionnaire was developed and used for data collection, including demographic, clinical, epidemiological, socioeconomic and environmental variables. In order to ensure standardization of field procedures, a manual with rules and concepts was developed to guide interviewers on how to correctly fill in this instrument.⁹

Data collection was carried out at daycare centers by means of interviews with mothers or guardians, anthropometry, and blood collection via digital puncture in the children. All procedures were standardized and tested in a pre-test stage of the project by a multiprofessional research team composed of students of the graduate programs in Pediatrics and Nutrition at Universidade Federal de São Paulo (UNIFESP), Brazil.

Hemoglobin concentration was determined using a HemoCue® β Hemoglobin Photometer portable hemoglobinometer, which is comparable to the standard laboratory techniques for measurement of hemoglobin levels.¹⁰ Anemia was defined as hemoglobin concentration below 11g/dL.¹¹

Children were weighted on a Filizola™ pediatric digital scale, BP Baby model, with minimum capacity of 125 g, maximum of 15 kg and graduated to each 5 g. Height was measured using an anthropometric ruler with a movable cursor, of the Brazilian Society of Pediatrics, graduated to each 0.5 cm up to 120 cm. Anthropometric measurements were performed following internationally-recommended procedures. Z scores were used to quantify nutritional deviations; negative weight gain was defined as the difference less than or equal to zero z score of the relationship weight/age between birth and participation in the surveys. The reference pattern age/sex herein adopted was that from the National Center for Health Statistics (NCHS), of 1978.¹²

Completed questionnaires were evaluated regarding their internal consistency. The data collected were entered on databases, with double typing and subsequent validation in order to correct errors. The Epi-Info™ 2000¹³ and Stata 10.0¹⁴ software packages were used for statistical analysis.

Univariate and bivariate descriptive consistency and statistical analyses were performed. The chi-square test was used to quantify chances in the associations.¹⁵

To control confounding variables, a multiple logistic regression model was adjusted to odds ratio (OR) estimates for risk factors between groups of children with and without anemia.¹⁶ Variables with level of significance less than 0.20 were selected for the logistic model-building and a maximum value of 0.05 indicated statistically significant associations; these criteria determined inclusion in the final model.

Among the socioeconomic variables which indicate effects of structural processes on the society and family,¹⁷ mother's age less than 28 years, based on the sample median, and per capita income below half minimum wage, considered a condition of extreme social deprivation, were identified to compose the final model because they showed $p < 0.05$ when associated with anemia, and also because they expressed residential characteristics, purchasing power and availability of supplies per family unit. Presence of one or more siblings under 5 years of age, a variable used in clinical investigations, also showed statistically significant risk association with anemia; however, this variable was not used due to its perfect collinearity with the variable per capita income below half minimum wage. Exclusive breastfeeding less than 2 months, considered an inadequate feeding condition in the first year of life and which indicates exposure conditions to the child immediate environment, was the third variable selected. Of the variables indicating individual child processes (biological factors, nutritional status and morbidity), the variables based on the sample median – age less than 17 months and negative weight gain – showed statistically significant association with anemia, the latter being selected to compose the final model. Daycare center attendance less than 180 days did not compose the final model because, when included in the model, this variable had its statistical significance weakened, not meeting the permanence criteria.

Due to difficulties in using the results of the logistic models in diagnostic and care practice, we calculated post-test probabilities relating anemia to isolated risks and combined in two, three, four and five risks. Post-test probabilities were calculated from a 50% pre-test probability, indicated for Brazilians under 5 years of age, and from the application of likelihood ratios to the interpretation of diagnostic data. Associations that caused major changes in the post-test probability in relation to the pre-test were considered useful in the diagnostic investigation of the event under study.¹⁸

The project was approved by the Research Ethics Committee of UNIFESP.

Children with nutritional disorders, including anemia, were referred to outpatient follow-up in the Nutrition health care unit of the UNIFESP Department of Pediatrics.

Results

The mean age of the children studied was 17 months, ranging from 4 to 29. Prevalence of anemia was 43.6% (95%CI 39.1-48.1). The number of children born prematurely, with low birth weight and receiving oral iron therapy was, respectively, 47 (9.9%), 47 (9.8%) and 22 (4.6%).

Table 1 shows data on the prevalence of anemia in children who presented or not the risk factors under study with their respective OR and 95% confidence intervals and post-test probability based on the calculation of likelihood ratios.

Thus, we can observe that children under 17 months of age are 2.5 times more likely to present anemia when compared to those at an older age. A value of $p < 0.001$ indicates that the odds of such risk be a result of chance is less than 1/1,000. Post-test probability indicates that, if the expected prevalence in the same-age infant population (pre-test probability) is 50%, when considering children under 17 months of age in clinical history, diagnostic probability increases to 61.5%. The same is valid for the interpretation of the other risk factors herein presented.

Figure 1 shows the final logistic model adjusted for anemia risk factors, with the five OR of the variables that remained in its final composition and their respective confidence intervals. Figure 1 also demonstrates that the following variables are identified as statistically significant independent risks: mother's age less than 28 years, per capita income below half minimum wage, exclusive breastfeeding less than 2 months, negative weight gain and child's age less than 17 months with OR around 2.0.

Table 2 shows data on the prevalence of anemia in children who presented or not the five risk factors selected for the logistic model-building, combined, respectively, in concomitance of two, three, four or five of these conditions, analyses of their effects ordered by statistical level of significance and post-test probabilities.

Therefore, as we can read on the first line of this table, if in clinical history the child is noticed to be less than 17 months old (A) and belongs to a family with per capita income below half minimum wage (D), post-test probability increases to 71.5%. When, in addition to these two situations, the child presents the other three identified risk factors (B, C and E), post-test diagnostic probability increases to 100%, as indicated on the last line of the same table.

Figure 2 shows variability and trend lines of post-test probabilities evidenced in the association of isolated and combined risk factors for anemia. This information summarizes the data shown in Table 2 with the aim of facilitating visualization of the increase in diagnostic probabilities when a larger number of risk factors are considered concomitantly.

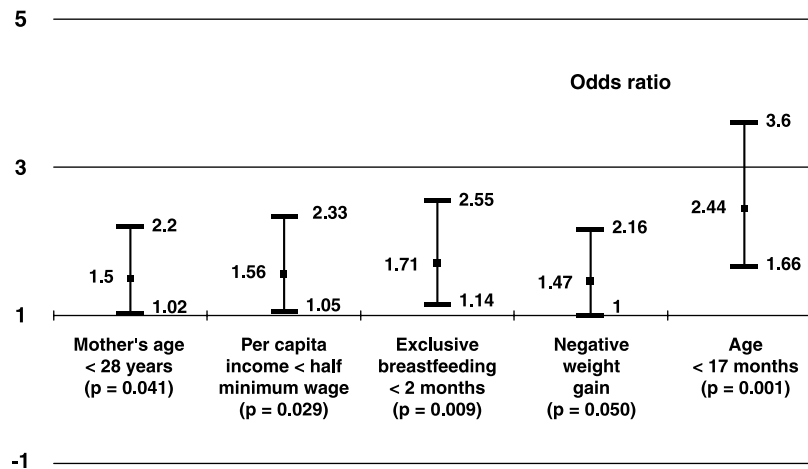


Figure 1 - Multiple logistic regression of anemia risk factors in children attending the nurseries of public and philanthropic daycare centers (São Paulo, Brazil, 2004 and 2007)

Table 1 - Prevalence, OR with respective confidence intervals and post-test probability for anemia risk factors in children attending public and philanthropic daycare centers (São Paulo, Brazil, 2004 and 2007)

Risk factors	n	Anemia prevalence n (%)	OR (95%CI)	p*	P (%)
Age (months)	482				
< 17	228	126 (55.3)	2.50 (1.73-3.62)	< 0.001	61.5
≥ 17	254	84 (33.1)	1.00		
1 or more siblings < 5 years old	481				
Yes	168	92 (54.8)	2.03 (1.39-2.97)	< 0.001	61.2
No	313	117 (37.4)	1.00		
Exclusive breastfeeding (months)	472				
< 2	166	86 (51.8)	1.74 (1.19-2.54)	0.004	58.8
≥ 2	306	117 (38.2)	1.00		
Daycare center attendance (days)	480				
< 180	204	103 (50.5)	1.64 (1.13-2.36)	0.008	56.9
≥ 180	276	106 (38.4)	1.00		
DifWAZ (measurement at birth)	479				
≤ zero	239	116 (48.5)	1.52 (1.05-2.18)	0.024	55.2
> zero	240	92 (38.3)	1.00		
Per capita income < half minimum wage	477				
Yes	177	89 (50.3)	1.54 (1.06-2.24)	0.024	56.7
No	300	119 (39.7)	1.00		
Mother's age < 28 years	479				
Yes	234	112 (47.9)	1.42 (0.99-2.05)	0.055	54.5
No	245	96 (39.2)	1.00		
Low birth weight (< 2,500 g)	479				
Yes	47	17 (36.2)	0.72 (0.38-1.34)	0.291	42.2
No	432	191 (44.2)	1.00		
Prematurity (< 37 weeks)	474				
Yes	47	20 (42.6)	0.95 (0.52-1.75)	0.871	48.7
No	427	187 (43.8)	1.00		

95%CI = 95% confidence interval; DifWAZ = difference in weight/age z score; OR = odds ratio; P = post-test probability from 50% pre-test probability.

* Non-corrected chi-square test.

Table 2 - Prevalence, OR with respective confidence intervals and post-test probability for risk factors combined in pairs, trios, quartets or quintets related to anemia in children attending the nurseries of public and philanthropic daycare centers (São Paulo, Brazil, 2004 and 2007)

Risk factors	n	Anemia prevalence n (%)	OR (95%CI)	p*	P (%)
A, D	229				
A + D	76	46 (60.5)	4.19 (2.34-7.50)	< 0.0001	71.5
no A + no D	153	41 (26.8)	1.00		
A, B	247				
A + B	78	50 (64.1)	4.13 (2.34-7.29)	< 0.0001	72.1
no A + no B	169	51 (30.2)	1.00		
A, E	249				
A + E	114	69 (60.5)	3.52 (2.08-5.94)	< 0.0001	66.0
no A + no E	135	41 (30.4)	1.00		
A, C	253				
A + C	120	70 (58.3)	3.50 (2.08-5.90)	< 0.0001	65.3
no A + no C	133	38 (28.6)	1.00		
B, C	232				
B + C	77	41 (53.2)	2.39 (1.37-4.19)	0.002	63.9
no B + no C	155	50 (32.3)	1.00		
C, D	243				
C + D	89	50 (56.2)	2.31 (1.35-3.93)	0.002	62.7
no C + no D	144	55 (35.7)	1.00		
B, E	262				
B + E	88	52 (59.1)	2.31 (1.37-3.89)	0.002	63.4
no B + no E	174	67 (38.5)	1.00		
C, E	251				
C + E	122	64 (52.5)	2.13 (1.28-3.55)	0.003	59.3
no C + no E	129	44 (34.1)	1.00		
B, D	287				
B + D	72	33 (45.8)	1.72 (1.00-2.96)	0.005	59.8
no B + no D	215	71 (33.0)	1.00		
D, E	229				
D + E	79	41 (51.9)	2.16 (1.24-3.77)	0.006	62.1
no D + no E	150	50 (33.3)	1.00		
A, C, E	136				
A + C + E	68	44 (64.7)	6.48 (3.03-3.84)	< 0.0001	70.5
no A + no C + no E	68	15 (22.1)	1.00		
A, B, E	134				
A + B + E	46	33 (71.7)	6.40 (2.90-4.12)	< 0.0001	76.9
no A + no B + no E	88	25 (28.4)	1.00		
A, B, C	124				
A + B + C	36	24 (66.7)	6.38 (2.73-4.91)	< 0.0001	77.8
no A + no B + no C	88	21 (23.9)	1.00		
A, C, D	120				
A + C + D	39	25 (64.1)	5.45 (2.38-2.45)	< 0.0001	74.8
no A + no C + no D	81	20 (24.7)	1.00		
A, D, E	112				
A + D + E	30	19 (63.3)	5.35 (2.18-3.14)	< 0.001	76.4
no A + no D + no E	82	20 (24.4)	1.00		
A, B, D	135				
A + B + D	27	16 (59.3)	5.09 (2.09-2.42)	< 0.001	77.5
no A + no B + no D	108	24 (22.2)	1.00		
B, C, E	132				
B + C + E	46	27 (58.7)	3.11 (1.48-6.53)	0.002	67.5
no B + no C + no E	86	27 (31.4)	1.00		
B, D, E	141				
B + D + E	32	18 (56.3)	3.39 (1.50-7.65)	0.003	71.3
no B + no D + no E	109	30 (27.5)	1.00		
B, C, D	141				
B + C + D	32	17 (53.1)	3.13 (1.39-7.06)	0.005	70.0
no B + no C + no D	109	29 (26.6)	1.00		
C, D, E	122				
C + D + E	45	23 (51.1)	2.17 (1.02-4.62)	0.042	61.7
no C + no D + no E	77	25 (32.5)	1.00		
A, B, C, D	72				
A + B + C + D	11	9 (81.8)	16.62 (3.19-86.53)	< 0.0001	91.1
no A + no B + no C + no D	61	13 (21.3)	1.00		
A, B, C, E	72				
A + B + C + E	26	19 (73.1)	11.16 (3.60-34.62)	< 0.0001	81.0
no A + no B + no C + no E	46	9 (19.6)	1.00		
A, B, D, E	72				
A + B + D + E	11	8 (72.7)	10.89 (2.50-47.33)	< 0.001	87.3
no A + no B + no D + no E	61	12 (19.7)	1.00		
A, C, D, E	58				
A + C + D + E	18	12 (66.7)	8.00 (2.29-27.90)	< 0.001	79.2
no A + no C + no D + no E	40	8 (20.0)	1.00		
B, C, D, E	76				
B + C + D + E	17	10 (58.8)	3.84 (1.25-11.81)	0.015	73.3
no B + no C + no D + no E	59	16 (27.1)	1.00		
A, B, C, D, E	38				
A + B + C + D + E	6	6 (100)	Not defined	< 0.001	100.0
no A + no B + no C + no D + no E	32	6 (18.8)	1.00		

95%CI = 95% confidence interval; A = age < 17 months; B = exclusive breastfeeding < 2 months; C = difference \leq zero in weight/age z score (measurement at birth); D = per capita income < half minimum wage; E = mother's age < 28 years; OR = odds ratio; P = post-test probability from 50% pre-test probability.

* Non-corrected chi-square test.

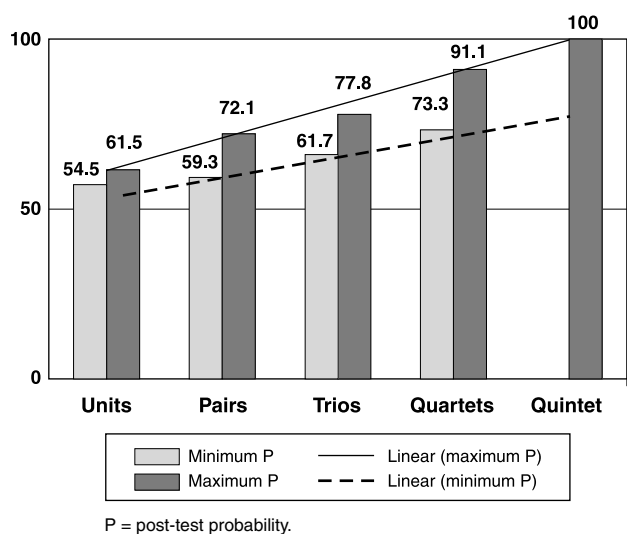


Figure 2 - Variability and trend lines of post-test probabilities resulting from the association of isolated and combined risk factors for anemia in children attending the nurseries of public and philanthropic daycare centers (São Paulo, Brazil, 2004 and 2007)

Discussion

The high prevalence of anemia in the infant population remains increased in all Brazilian regions.¹⁹ Similar alarming rates were found in the present study in an infant population attending daycare centers in the city of São Paulo, Brazil.

The iron deficiency status bears the potential to develop motor and cognitive functional limitations and social and emotional behavioral changes,^{20,21} which underscores the importance of the health professional to suspect, identify and immediately treat this nutritional deficiency. In order to do that, understanding the epidemiological profile of anemia is of paramount importance. Biological, socioeconomic, cultural and nutritional factors are closely involved, featuring a development process that results from several determining conditions.²² In this study, this complex condition motivated the statistical analysis of isolated and combined risks, leading to the identification of situations in which children were more likely to have or develop anemia, even from the first years of life.

Despite the results found in other studies, this investigation did not identify a statistically significant association between prematurity and/or low birth weight and anemia. This fact may result from the weakening of the influence of this variable over time, since the median age of the sample under study was 17 months.^{17,19,22} Worth mentioning that data on the umbilical cord of the children herein studied were not collected, which may have limited the value of our findings as the early clamping following birth has been considered an important determinant of anemia according to several studies.²³

The present study identified a statistically significant association of seven risk factors. These factors, when isolated, determine that a child is 1.4 to 2.5 more likely to have anemia when compared to children without these risk conditions. Among these risk situations, we highlight age less than 17 months, whose analyses (isolated and combined) resulted in the greatest chances and probabilities of the occurrence of anemia. The identified association indicates that younger age groups are more susceptible to the development of anemia, confirming findings from previous studies.^{3,24,25} This fact may be explained by the high demand for iron necessary to ensure physical growth, which is accelerated mainly during the first year of life.³

In a similar way, children with a history of weaning beginning before 2 months of age showed greater risk to develop anemia. This situation emphasizes the importance of breast milk iron, regardless of other milks, and meets the physiological needs of infants under 6 months of age on exclusive breastfeeding.²⁶ The identification of anemia risks in children of mothers under 28 years of age, when compared to children of older mothers, suggests that the younger mothers are less prepared to care for their children concerning their nutritional needs, which may reflect a lack of appropriate levels of information, support, resources and opportunities to adequately care for their children.

The anthropometric indicator used in this study, which is not necessarily an indicative of current malnutrition, but could translate an unsatisfactory weight gain from birth up to carrying out the surveys, showed a statistically significant association with anemia in both the bivariate analysis and the final model. This situation demonstrates that children with negative weight gain in z scores, based on the relationship weight/age throughout the first years of life, are more likely to develop iron deficiency, suggesting that situations of possible food restriction and/or metabolic loss result in a limited storage of this mineral. This fact is explained by the greater need for bioavailable iron at this age group and by the limitations in the supply of this mineral when iron-enriched foods are not available.³

Among the situations favorable to the occurrence of iron deficiency is the socioeconomic condition of lower income classes.²⁷ Although the homogeneity of the population herein studied hinders comparisons, the situation of per capita income below half minimum wage can be considered a risk factor for anemia. This evidence indicates that, even among underprivileged groups, children from families which suffer from excessive lack of financial resources are at greater risk to develop anemia, reflecting their actual situation of food insecurity.

The analysis of the five risk situations selected for the logistic model showed the proportional increase in the probability of the occurrence of anemia when two or more of these situations happened simultaneously. The probability of the occurrence of anemia, which ranged from 54.5 to

61.5% in the presence of one risk factor, reached values greater than 90% when four risk factors were considered together.

In the association of variables combined in pairs, we observed that associations combining lower child's age with shorter time of exclusive breastfeeding and lower child's age with lower per capita income stood out, resulting in post-test probabilities greater than 70%. When the combined presence of these three variables was considered, post-test probability of anemia reached 77.5%, showing that children simultaneously at a younger age group, with low income and short period of exclusive breastfeeding are more likely to have decreased circulating hemoglobin. In a similar way, when negative weight gain was added to these variables, post-test probability reached 91.1%, suggesting that children at a younger age group, early weaned, from very low-income families and with weight loss proportional to nutritional status at birth are highly susceptible to anemia.

Worth mentioning that all six children who simultaneously had the five risk factors suffered from anemia. Although this modest occurrence does not allow a statistical association, this result pointed to the trend line of 100% probability of anemia.

Although the sample studied included a small percentage of children on oral iron therapy and showed specific characteristics of an institutionalized and uniform socioeconomic level, in addition to the sample nonrandomized design, post-test probabilities with the presence of one or more of the five identified risk factors, selected and controlled in the logistic model, provided a simple and rapid tool for suspicion of the occurrence of anemia in children both in clinical practice and population screening.

These risk factors were only statistically confirmed in the present study, once their determination processes were already indicated in previous investigations; however, this information is easily obtained from the patient history and physical examination, directing the decision-making process to the prevention and treatment of this specific mineral deficiency.

In this context, with the repeated characterization of anemia as a serious public health problem by the literature,²⁸ especially in developing countries such as Brazil, the role of the health professional in the fight against iron deficiency and anemia in children under 2 years of age is of utmost importance.

The data found in the present study reinforce the need to adopt prevention guidelines and to improve the living conditions of the low-income Brazilian population. Thus, the permanent clinical and pedagogical practice should encourage adequate breastfeeding, enrichment of low-cost foods available in the market, supply of

oral iron supplementation and promotion of nutrition education through direct contact with educators, mothers and guardians.¹

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