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REVIEW ARTICLE

Recommendations for the management of iron deficiency and iron deficiency anemia in pediatrics: an update

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Abstract

To identify risk factors related to a higher prevalence of iron deficiency and iron deficiency anemia and propose strategies for prevention. A literature review was conducted by 22 people from the scientific departments of nutrology and hematology at SBP. The risk factors for the development of iron deficiency anemia were low maternal reserve (pregnant woman with anemia without adequate treatment, breastfeeding woman without adequate iron supplementation, short interval between pregnancies, malnutrition), decrease in iron supply (umbilical cord clamping before one minute, vegetarianism, whole cows milk), newborn with low iron reserve (prematurity, low weight) and iron malabsorption (decreased gastric acidity, malabsorption syndrome). As a strategy to prevent the repercussions of iron deficiency (cognitive alterations, short stature, frequent infections), we recommend starting iron prophylaxis in full-term children, regardless of the type of diet, at 90 days of life; and for those with risk factors for iron deficiency anemia, at 180 days of life. The laboratory diagnosis of iron deficiency should be made with serum ferritin and CRP levels (to rule out infection) and the diagnosis of iron deficiency anemia with concomitant red blood cell count and reticulocyte. Pediatricians should be aware of the importance of iron deficiency anemia in Brazil and the need to prevent iron deficiency, especially at the beginning of life, avoiding the long-term consequences of this deficiency that have repercussions on child neurodevelopment.

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INTRODUCTION

The World Health Organization (WHO) considers it to be anemia when the hemoglobin (Hb) concentration is below two standard deviations of the average Hb of the population of the same age, sex and living at the same altitude. Therefore, the normal Hb value varies in the pediatric population, mainly depending on age[1,2]. Population studies use the Hb parameters used by the WHO.

Iron deficiency and iron deficiency anemia in childhood and adolescence remain a public health problem in Brazil[3-5]. A systematic review published in 2009 found a high prevalence (53%) of iron deficiency anemia in children between six months and five years of age, considering the Hb value = 11 g/dL as a cut-off point[3]. More recent Brazilian data also demonstrate high prevalence rates of anemia in children. In the National Child Food and Nutrition Study (ENANI), the prevalence of anemia in children under five years of age was 10%; 18.9% in those between six and 23 months of age and 5.6% among 24 and 59 months of age[5]. The prevalence of iron deficiency anemia was 3.6%, being higher in the North region (6.9%) and among children aged six to 23 months (8%)[5]. A meta-analysis with 134 articles published between 2007-2020 found an estimated prevalence of 33% of anemia in healthy Brazilian children under seven years of age[4]. These studies highlight the high number of children exposed to the consequences of iron deficiency on physical, cognitive, behavioral and immunological development. The higher prevalence of iron deficiency anemia in infants is worrying because it is precisely during this period that more substantial growth of the central nervous system (CNS) is observed and the sequelae of anemia and iron deficiency may be more relevant and serious[6-8].

The objective of this review was to identify groups and risk factors related to the higher prevalence of iron deficiency and iron deficiency anemia in children, review the health repercussions of iron deficiency and iron deficiency anemia and identify prevention and treatment strategies for iron deficiency in the body.

METHODS

A group composed of 22 Brazilian pediatricians, specialists in iron deficiency anemia in pediatrics, members of the Scientific Department of Hematology and Hemotherapy (8 holders and 3 participants) and Nutrology (8 holders and 3 participants) of the Society's 2019-2022 management Brazilian Society of Pediatrics (SBP) came together to work towards meeting the proposed objectives.

The process was established in three stages starting in December 2020. In the first, the group evaluated the content of the "consensus on iron deficiency anemia: more than a disease, a medical emergency!", published in 2018 by SBP. Subsequently, essential points for review were defined, such as definitions, diagnostic criteria and treatment and prevention strategies for iron deficiency anemia. To search for updated information, group members individually carried out literature reviews in the suggested databases: Medline, Scopus, Embase, Web of Science, Lilacs and Scielo. In the second stage, seven successive online meetings took place to discuss each issue raised by members, according to individual searches. Differences between scientific articles were considered and the search for consensus was the main objective. Each topic was studied and evaluated together. Ways of expressing ideas were agreed after considerations raised by the group. All members had the same right and voice in the virtual meetings to prepare the final text, which fundamentally had scientific evidence as a basis for support. For the points where there were still gaps in knowledge, Brazilian and international institutional recommendations and protocols, the opinions and experiences of the participants and the search for a single and consensual direction were considered. After 9 months that included virtual meetings and exchanging emails with considerations and ideas, the final stage took place. The last meeting was held in September 2021, which made it possible to close the discussions and organize the final textual structure with the unanimous approval of the entire group.

RESULTS AND DISCUSSION

Groups and risk factors for iron deficiency

The prevalence of anemia in pregnancy is approximately 40%, more than 50% of which is due to iron deficiency[9]. Iron needs during pregnancy are six times higher, requiring the use of maternal reserves and medication supplementation for the adequate development of the fetus. Maternal iron deficiency anemia influenced the infant's Hb values at six months of age, even in those who were exclusively breastfed[9,10]. Maternal anemia is associated with reduced birth weight and increased risk of maternal mortality. Children of mothers with anemia may be more likely to have iron deficiency and anemia early in life[10].

Newborns (NB) with low birth weight and premature babies are at higher risk of iron deficiency due to the absence of endogenous iron stores, but also those born at term and with adequate weight, with inadequate iron intake, due to high metabolic demand or illness, or inadequate absorption or excessive loss of iron. Therefore, iron stores in children at 4-6 months of age may not be sufficient to meet their nutritional needs[1,11].

Iron deficiency anemia in children under two years of age and in adolescents occurs due to the high metabolic need for rapid growth and development, associated with a diet poor in iron[12]. Another risk factor in adolescent girls is menstrual loss[2,13]. For infants, the risk of iron deficiency anemia increases when they live with one or more children under five years of age, with the introduction of fruits and vegetables in complementary foods after eight months of age, malnutrition, vitamin A deficiency and folic acid, signs of an inflammatory process and previous hospitalization[14]. Socioeconomic vulnerability, probably due to inadequate

nutrition and precarious sanitary conditions[15,16], as well as obesity are also associated with a higher prevalence of iron deficiency anemia[17,18].

The use of fresh, unmodified cow's milk, in powder or liquid form, before 12 months of age, may be a risk factor for iron deficiency[19,20]. And, especially in Brazil, as demonstrated in a recent study, the presence of low bioavailability iron in the diet is an important risk factor[21].

Chart 1 describes the main risk factors and their causes for iron deficiency anemia in children and adolescents[2,10,11,13,18,19,22,23].

Health repercussions of iron deficiency and iron deficien anemia

Iron deficiency indicates a state of negative iron balance, that is, when the iron reserve cannot meet the body's necessary demand to guarantee respiratory function (Hb synthesis), the functioning of the immune system, growth and development[22]. In cases where iron deficiency is associated with anemia, we have iron deficiency anemia that affects growing age groups and compromises brain development[24].

The first thousand days of life (from conception to two years of age) are considered a critical period for growth and development because there is an increased susceptibility to nutritional deficiencies, which can compromise the CNS[25]. In addition to being fundamental for the production of Hb, iron is one of the main nutrients essential for myelination and the structural and functional formation of neurotransmitter pathways. Furthermore, it participates in the energy metabolism of the hippocampus and the neuronal network growth[2,23].

Since the prenatal period, iron deficiency has important and long-term deleterious repercussions on the development of children's cognitive, behavioral, language and psycho-emotional and motor skills[6,7], and the possible negative impact can persist for decades even after early treatment, especially in children who are understimulated or of low social and economic status[7,26,27].

Iron deficiency in childhood also predisposes to dental cavities, less discrimination and identification of odors, changes in non-specific immunity, changes in taste and appetite, altered response to metabolic stress and changes in audiovisual development[28-30].

Chart 1. Risk factors and their causes for iron deficiency anemia in children and adolescents.

Risk Factor	Associated Cause
Low maternal reserve	Multiple pregnancies Short interval between pregnancies Iron-deficient maternal diet Blood loss Not taking iron supplements during pregnancy
Increased metabolic demand	Prematurity Infants Girls with heavy menstrual losses Competitive athletes
Supply shortage	Umbilical cord clamping before one minute of life Prolonged exclusive breastfeeding Complementary feeding with foods low in iron or low in bioavailability Consumption of cow's milk before one year of age Consumption of infant formula with low iron content or insufficient quantity of infant formula Vegetarian diets without guidance from a doctor/nutritionist
Blood loss	Traumatic or surgical Gastrointestinal bleeding: inflammatory bowel disease, colonic polyposis, non-steroidal anti-inflammatory drugs, Helicobacter pylori infection, worms (strongyloides, necator, hookworm), allergic enteropathies/colitis, schistosomiasis Gynecological bleeding: menorrhagia, intrauterine devices Urological bleeding: schistosomiasis, glomerulonephritis, renal trauma Pulmonary hemorrhage: tuberculosis, lung malformation, idiopathic pulmonary hemosiderosis, Goodpasture syndrome Blood dyscrasias Malaria COVID-19
Poor iron absorption	Malabsorption syndromes: celiac disease, inflammatory bowel disease Atrophic gastritis Gastric surgery Reduction of gastric acidity: antacids, H2 blockers, proton pump inhibitors Iron-refractory iron deficiency anemia Obesity
Low adherence to prophylactic supplementation with medicated iron	

Actions to prevent iron deficiency anemia

Actions to prevent iron deficiency anemia provide for exclusive breastfeeding up to six months of age and supplementary breastfeeding up to two years of age, associated with universal access to adequate nutrition by the mother during pregnancy and lactation and by the infant, increasing the consumption of foods that are sources of iron and foods that increase the bioavailability and absorption of iron when introducing complementary foods[2,11].

Other preventive actions for iron deficiency anemia include umbilical cord clamping time between 1-3 minutes, adequate guidelines for complementary feeding of infants and adequate use of infant formulas, appropriate nutritional guidelines for families with specific eating routines, such as vegetarianism or families whose children eat all meals at school, reinforce pediatric consultation during prenatal care,[31] encourage neonatal screening tests to analyze other causes of anemia.[11] Another protective strategy against iron deficiency and the development of iron deficiency anemia is not to use fresh, unfortified, powdered or liquid cow's milk before 12 months, limiting its consumption to 500 mL/day after 12 months.[19,20]

It is important to remember that in full-term newborns with adequate weight, 80% of the iron is accumulated during the third trimester of pregnancy. Thus, premature and low weight children are born with lower iron reserves. Maternal conditions such as anemia, high blood pressure with impaired intrauterine growth and diabetes mellitus can lead to low iron stores in both full-term and premature newborns[2,32]. Prophylactic iron supplementation in adequate doses in pregnant and breastfeeding women is sufficient to increase Hb and iron stores in the fetus and infant, thus reducing the risk of anemia in children between four and 23 months[33]. Maternal anemia favors anemia in infants at six months of age, even when exclusively breastfed[34,35].

Full-term newborns generally have sufficient iron stores until four to six months of age[2]. Therefore, exclusive breastfeeding protects infants from iron deficiency and iron deficiency anemia in the first four months of life. After this age, according to the literature, there is an increase in the rates of anemia and iron deficiency, adding to the evidence that supports the monitoring of iron levels in exclusively breastfed children, with greater weight gains from the age of four months[34]. Iron supplementation also improves visual acuity and Psychomotor Development Indexes (Bayley Scale) at 13 months. The American Academy of Pediatrics recommends that both full-term babies who are exclusively breastfed and those who are not exclusively breastfed should receive iron supplementation at a dose of 1 mg of elemental iron/kg/day from four months of life[32]. In Brazil, Resolution - RDC No. 150, of April 13, 2017, defines as a public policy for the prevention of iron deficiency anemia the mandatory iron supplementation for pregnant women, lactating women and infants, and the fortification of foods (wheat and corn flour)[36].

Drug prophylaxis of iron deficiency

According to the WHO guidance for regions with a prevalence of iron deficiency anemia higher than 40%, the dose of prophylactic supplementation with elemental iron should be adjusted to the age group. Thus, the WHO recommends a dose of 10–12.5 mg of elemental iron/day for children between six and 23 months and 30 mg/day for children between 24 and 59 months[2,11]. For pregnant women, the prophylactic recommendation is 40 mg/day of elemental iron for non-anemic women and 60-120 mg/day for pregnant women with anemia, for at least 60 days[37].

A) Full-term newborns

The age at which drug prophylaxis for iron deficiency should begin should be, depending on the infant's history, 90 or 180 days of life and is based on the following evidence from the literature:

- Maternal conditions such as anemia, high blood pressure with impaired intrauterine growth and diabetes mellitus can also lead to a decrease in iron reserves in full-term newborns[32].
- Start iron supplementation before iron stores decrease, since exclusive breastfeeding protects infants from iron deficiency and iron deficiency anemia in the first 90 days of life[34] and full-term newborns have sufficient iron stores until four to six months of age[11,32].
- Iron supplementation in children between one and six months of age who are exclusively breastfed results in higher Hb at six months of age when compared to infants who did not receive prophylactic iron[32].
- The amount of iron in standard infant formula for full-term infants is 12 mg/L. Thus, based on a standard daily intake of 150 mL/kg of milk, newborns receive 1.8–2.2 mg/kg/day of low bioavailability iron[32].
- As CNS development occurs substantially in infants, the possible sequelae of iron deficiency anemia are more serious[8,38-40], and it is the pediatrician's duty to ensure the adequate neurological development of their patients. Once established, cognitive impairment resulting from a lack of iron may not be reversed with iron replacement[11,32].

B) Premature newborns

Prophylactic iron supplementation in premature newborns should be started at 30 days of age and maintained at least until they reach two years of age, based on the following facts:

- Iron deposition occurs in the third trimester of pregnancy[32].
- There is a high demand for iron for postnatal growth[41].
- Around 25–85% of premature newborns develop iron deficiency, with or without anemia[42].
- Umbilical cord serum iron and serum ferritin concentrations are lower in premature infants when compared to full-term newborns[43].

● The amount of iron in standard infant formula for premature infants is 14.6 mg/L. Even when receiving formula enriched with iron, up to 14% develop iron deficiency in the first year of life[32].

The survival of premature newborns with very low birth weight has increased thanks to advances in neonatology, including therapy with transfusion of packed red blood cells which, even with restrictive indications, can lead to mild to moderate hepatic iron overload[41]. There are no specific guidelines regarding iron supplementation in premature infants with increased serum ferritin. Our recommendation is that evaluation with iron, ferritin and transferrin saturation index be carried out immediately after discharge and, subsequently, as necessary. If in doubt, one can be referred to a pediatric hematologist.

C) Literature analysis

Considering the researched literature, in exclusively breastfed infants, without risk factors for iron deficiency, prophylactic iron supplementation can be recommended from 180 days of life until the end of the second year (Chart 2, Figure 1). However, if there are risk factors, prophylactic iron supplementation begins at 90 days, regardless of the type of food (Chart 3, Figure 1). Remembering that after the age of two it is important to monitor one's diet as part of the prevention of iron deficiency anemia.

Clinical and laboratory diagnosis of iron deficiency with or without anemia

Iron deficiency occurs in three evolutionary stages. In the first, there is a depletion of iron stores (ferritin), with a decrease in iron deposits in the body (liver, spleen and bone marrow). In the second stage (iron deficiency without anemia), iron stores are depleted, but the patient does not yet manifest anemia. In the third stage (iron deficiency anemia), after a long period of iron deficiency, there is a drop in Hb synthesis with consequent microcytic and hypochromic anemia[45]

The clinical manifestations of iron deficiency occur in the three stages of the disease. However, it is in iron deficiency anemia that clinical repercussions such as paleness, apathy, tiredness and irritability are more frequent[2,46]. To avoid complications caused by chronic iron deficiency, we must prevent its deficiency in children. Specific laboratory tests provide a diagnosis for each of the three stages of iron deficiency (Chart 4)[2,47-49]. Serum ferritin must be evaluated depending on the presence or absence of infection and/or inflammation to define iron deficiency (Chart 5)[50].

In pediatrics, the normal Hb value and the Hb value considered as anemia vary with the age group[51,52]. The evaluation of reticulocytes (immature red cells without a nucleus) also helps in the diagnosis and the absolute reticulocyte count performed by flow cytometry is more accurate than manual counting (normal value 0.5-1.5%). Reticulocytosis suggests hemolysis (increased erythropoiesis) and reticulocytopenia suggests bone marrow hypoplasia/aplasia (production failure). Erythropoiesis in iron deficiency can still be assessed by mean reticulocyte volume and the fraction of immature reticulocytes[53]. The Hb content of reticulocytes (CHr) indirectly provides the iron available for the production of erythrocytes in the bone marrow and, therefore, its decrease is a strong indicator of iron deficiency[54]. Table 1 lists the mean and lower limit values for Hb, hematocrit (Ht), mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) according to age and sex and in Table 2, the automated values for reticulocyte count, immature reticulocyte fraction and mean reticulocyte volume.

Iron deficiency should be assessed with at least two parameters in addition to Hb[49]. The WHO assesses iron status in populations with Hb and serum ferritin and/or transferrin receptor[2]. The American Academy of Pediatrics recommends investigating iron deficiency from 12 months of age or, in children at risk for iron deficiency, at any time, with the diagnosis being made using Hb, serum ferritin and C-reactive protein (CRP) or CHr[32].

In the need for differential diagnosis or when there is no response to iron treatment, other tests must be evaluated. With the heel prick test (neonatal screening) it is possible to rule out sickle cell disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency. It is worth mentioning that thalassemia minor, a differential diagnosis of iron deficiency anemia, it is not identified in neonatal screening and requires hemoglobin electrophoresis for diagnosis. Other causes of microcytic hypochromic anemia in children are anemia of infection/inflammation, copper deficiency, sideroblastic anemia, and iron refractory iron deficiency anemia (IRIDA). To diagnose anemia, the reference value of the blood count parameters for each age must be used (Table 1). Once the diagnosis of iron deficiency or iron deficiency anemia has been defined, treatment must be immediate, with the best available medication, adequate control and for the necessary time.

A) Literature analysis

Considering the researched literature, laboratory investigation of iron deficiency with or without anemia

Chart 2. Recommendation for prophylactic iron supplementation in infants WITHOUT risk factors for iron deficiency.

Infants WITHOUT risk factors	
Situation	**Recommendation**
Full-term newborns, weight appropriate for gestational age, exclusively breastfed until the 6th Month.	1 mg of elemental iron/kg/day, starting at 180 days of life until the 24th month of life.

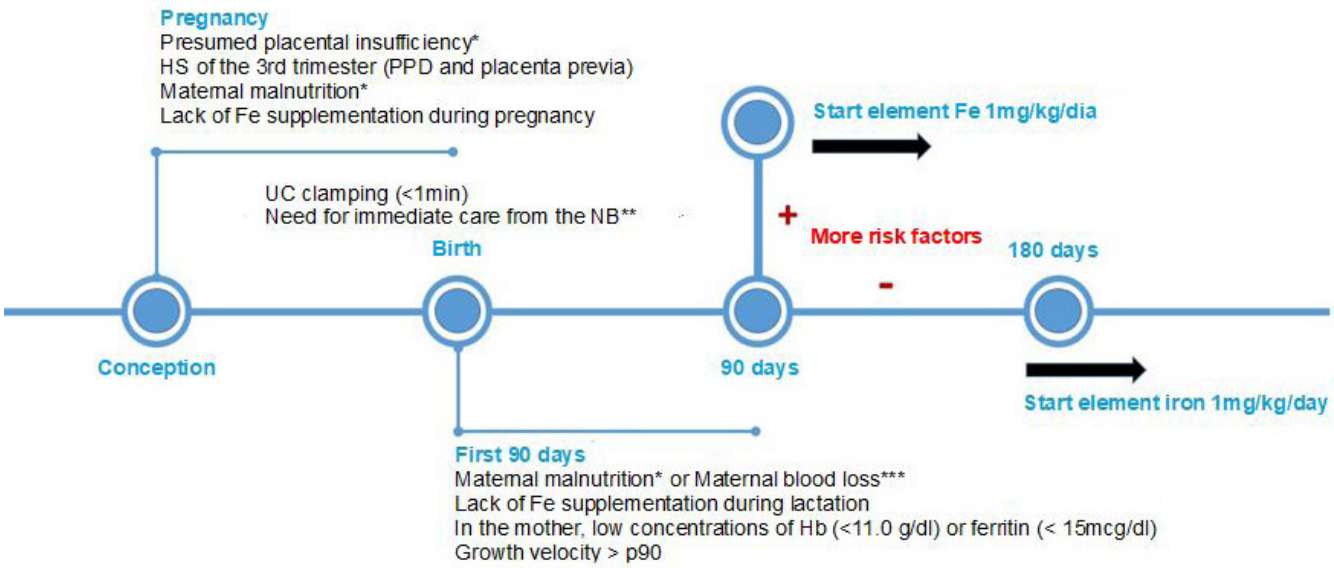

Figure 1. Infographic: Age at which medicated iron supplementation begins for exclusively breastfed infants, born at term and with adequate weight (≥ 2,500g), according to the presence or absence of risk factors for iron deficiency.
Source: SBP, 2021. 44

Chart 3. Recommendation for prophylactic iron supplementation in infants WITH risk factors for iron deficiency.

Infants WITH risk factors	
Situation	**Recommendation**
Full-term newborns, weight appropriate for gestational age, in exclusive breastfeeding	**1 mg of elemental iron/kg/day, starting at 90 days of life until the 24th month of life.**
Full-term newborns, appropriate weight for gestational age, regardless of the type of food	**1 mg of elemental iron/kg/day, starting at 90 days of life until the 24th month**
Full-term newborns weighing less than 2,500 g	**2 mg of elemental iron/kg/day, starting at 30 days of life, for one year. After this period, 1 mg/kg/day for another year**
Preterm newborns weighing more than 1,500g	**2 mg of elemental iron/kg/day, starting with 30 days of life for a year. After this period, 1 mg/kg/day for another year**
Preterm newborns weighing between 1,500 and 1,000 g	**3 mg of elemental iron/kg/day, starting at 30 days of life, for one year. After this period, 1 mg/kg/day for another year**
Preterm newborns weighing less than 1,000 g	**4 mg of elemental iron/kg/day, starting at 30 days of life, for one year. After this period, 1 mg/kg/day for another year**
Preterm newborns who received more than 100 mL of packed red blood cells during hospitalization	**They must be evaluated individually as they may not require iron supplementation at 30 days of age, but rather later.**

must be carried out at 12 months of age, since from the 6th month onwards iron reserves have already been exhausted and become dependent on food supply and prophylactic supplementation, which are not always appropriate. In children at risk for iron deficiency (Chart 6), the investigation should be carried out in the 4th month of life.

Children should be constantly monitored for possible causes of iron deficiency, especially if they do not take adequate iron prophylaxis, if they have recurrent infections, if they are irritable or if they sleep a lot.

To optimize the cost and the need for standardization of diagnostic tests to identify iron deficiency without anemia, where Hb is normal, at least the following tests are necessary:

1. Complete blood count: evaluation of Hb, hematimetric indices (MCV, HCM, RDW) and red blood cell morphology. In iron deficiency anemia, hypochromic (decreased HCM) and

Chart 4. Laboratory evaluation of the different stages of iron deficiency and serum ferritin cutoff values to define iron deficiency in apparently healthy and unhealthy individuals, by age group.

Laboratory assessment of the different stages of iron deficiency			
	Iron stocks depleted	Iron deficiency	Iron deficiency anemia
Red blood cell morphology (VCM, HCM, RDW)	Normal	Normal	↓ VCM* (microcytosis) ↓ HCM* (hypochromia) ↑ RDW
Ferritin	Reduced	Reduced	Reduced
Serum iron	Normal	Reduced	Reduced
TIBC	Normal	Increased	Increased
Transferrin saturation index **	Normal	Reduced	Reduced

Caption: MCH, mean corpuscular hemoglobin; RDW, red cell distribution width (measure of anisocytosis); TIBC, total iron binding capacity; MCV, mean corpuscular volume. *Vary with age ** Calculation of transferrin saturation index = (Iron/TIBC) x 100.

Chart 5. Ferritin values according to age and the presence or absence of infection 50.

Age	**Serum ferritin (mcg/dL)**	
	Healthy	With infection or inflammation
0-23 months	<12	<30
24-59 months	<12	<30
5 a <10 years	<15	<70
10 a <20 years	<15	<70

Table 1. Mean and lower limit values for Hb, Ht, MCV and MCHC according to age and sex.

Age	Hb (g/dL)		Ht (%)		MCV (fL)		MCHC (g/dL)	
	Mean	-2SD	Mean	-2SD	Mean	-2SD	Mean	-2SD
FTN	18.0	15.0	58	45	108	98	33	30
1 week	17.0	13.5	54	42	107	88	33	28
2 weeks	16.0	12.5	52	39	105	86	33	28
1 month	14.0	10.0	43	31	104	85	33	29
2 months	11.5	9.0	35	28	96	77	33	29
3 to 6 months	11.5	9.5	35	29	91	74	33	30
6 to 24 months	12.0	10.5	36	33	78	70	33	30
2 to 6 years	12.5	11.5	37	34	81	75	34	31
6 to 12 years	13.5	11.5	40	35	86	77	34	31
12 to 18 years	14,0	12,0	41	36	90	78	34	31
Female	14.0	12.0	41	36	90	78	34	31
Male	14.5	13.0	43	37	88	78	34	31
18 to 49 years	16,0	13,0	47	40	90	80	34	31
Female	14.0	12.0	42	37	90	80	34	31
Male	16.0	13.0	47	40	90	80	34	31

FTN: full-term newborn; Hb: hemoglobin; Ht: hematocrit; MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration; SD: standard deviation.

Source: adapted from Orkin et al., 2008; 51 Barone, 2006; 52 Bain 2016. 53.

microcytic (decreased MCV) red blood cells are observed, anisochromia (variation in the amount of paleness in the center of red blood cells), anisocytosis (variation in the size of red blood cells), elliptocytes (red blood cells with an oval shape), target red blood cells (zone of paleness in the center of the red blood cell), basophil stippling (aggregated ribosomes) and Howell-Jolly bodies (nucleus remains) in the severe form[51].

2. Serum ferritin: its use as a marker of the store depletion phase is essential because intervention in this phase can prevent cognitive deficits.

Table 2. VaAutomated values for reticulocyte count, immature reticulocyte fraction and mean reticulocyte volume.

Instrument	Reticulocytes (per mm3)	Fraction of immature reticulocytes (%)	Mean corpuscular volume (fL)
Cell-Dyn 4000	28,000-119,000	0.20-0.40	---
Sysmex XE-2100	27,000-99,000	0.02-0.11	---
Advia 120	33,000-104,000	0.06-0.20	100-114
ABX Pentra 120	30,000-105,000	0.09-017	91-111
Coulter LH 750	18,000-114,000	0.22-0.40	98-120

Source: adapted from Bain 2016. 53

Chart 6. Infants at risk for iron deficiency.

Premature < 37 weeks
Low birthweight
Pregnant women with iron deficiency anemia or without iron supplementation during pregnancy
Breastfeeding woman with iron deficiency anemia or without iron supplementation during lactation
Exclusive breastfeeding for more than six months of age
Exclusive breastfeeding for more than four months of age without iron prophylaxis
Interruption of breastfeeding and use of whole cow's milk or
complementary foods not fortified with iron or without iron-rich foods
Poor growth and inadequate nutrition, often in babies with
special health conditions or low socioeconomic status
Lead poisoning

3. C-reactive protein: to identify an infectious process, since ferritin is a non-specific inflammatory protein.

If there is a need for further investigation into the cause of the anemia, the patient should be referred to a pediatric hematologist.

TREATMENT FOR IRON DEFICIEN ANEMIA

Treatment planning for iron deficiency anemia should be based on confirming the diagnosis and etiology of the anemia, followed by correction of the primary cause and use of oral iron (dose of 3 to 6 mg of elemental iron/kg/day), divided or in doses, before meals, for six months. In severely malnourished patients, the dose of oral iron should be 3 mg of elemental iron/kg/day[55]. The addition of vitamin C, through supplements or juice, can increase iron absorption when using ferrous salt or other iron salts[47,56]. Treatment control should be carried out with a blood count 30-45 days after starting treatment, when an increase in Hb of at least 1.0 g/dL is expected[57]. If this increase in Hb does not occur, the cause of non-response must be identified. Confirmation of therapeutic success will occur with the normalization of Hb, MCV, HCM and serum ferritin, the measurement of which must be carried out at the end of the 6th month of treatment to ensure that iron stores have been replenished[58].

It is important to remember that the dose of iron depends on the salt used in the treatment. Therefore, the calculation of the elemental iron dose is not the same for the different commercially available iron compounds. Your choice must consider the absorption patterns of each salt, the degree of response in relation to treatment time and the lower occurrence of adverse events (AE). The use of chelate-bisglycinate salts or polymaltosated iron is suggested, both for the treatment of iron deficiency anemia and in prophylactic supplementation programs, with the aim of reducing iron AEs that cause low adherence to the program. In the absence of access to ferric salts, ferrous sulfate is the medication of choice, with monitoring of adherence to the program due to the high percentage of AE, even at low doses.

Therefore, when prescribing the prophylactic or therapeutic dose of iron, the leaflet of the chosen medication must be checked for the quantity in mg of elemental iron and the equivalent in drops or mL so that the dose calculation is correct. The ferrous sulfate available in the Public Healthcare System (SUS) varies greatly in iron concentration. As an example, the bottle purchased may have 0.56 mg of elemental iron in 1 drop and, in another purchase, the bottle may have 0.90 mg of elemental iron in 1 drop.

Iron should not be prescribed during infection because its intestinal absorption is reduced. If the patient is hospitalized, remember to prescribe iron upon discharge.

Guidance for parents and the correct management of iron AEs are essential for treatment compliance. The main AEs of ferrous sulfate are nausea, heartburn, epigastric pain, diarrhea, constipation and tooth stains. As strategies to improve treatment adherence, if the patient has AE, we must[58]:

- Divide the total recommended daily dose into two or three doses;

● Administer the medication during or after meals, remembering that in this situation the treatment will last longer because iron absorption is lower;

● Start therapy with a lower dose than recommended, gradually increasing according to the patient's tolerance and

● Change the medication to another iron base.

A) Iron deficiency anemia unresponsive to treatment

In the absence of the expected response to the treatment of iron deficiency anemia, correct treatment compliance must be assessed (correct administration of the medication, acceptance of the medication by the patient, lack of adherence due to AEs such as dark stools and/or teeth and/or abdominal pain) before changing medication. In addition to treatment with oral iron, intravenous iron replacement is recommended in exceptional cases, such as hospitalization for severe anemia after therapeutic failure of oral treatment, which is necessary.

The need for iron replacement due to blood loss, inflammatory bowel diseases, chemotherapy or dialysis or after gastric surgeries involving the small intestine, and an assessment from an experienced pediatric hematologist should always be requested[55].

CONCLUSION

Pediatricians must be aware of the importance of iron deficiency anemia in Brazil, which requires greater care for children to prevent iron deficiency, especially in the early stages of life. In this way, we avoid long-term consequences of this deficiency, with negative repercussions on children's neurodevelopment. Parents should be made aware of the importance of prophylaxis and adequate treatment of nutritional iron deficiency. Actions developed in childcare should be encouraged to reduce the high prevalence rates of anemia and iron deficiency in children. In this way, the motto is justified: IRON DEFICIENCY ANEMIA, MORE THAN A DISEASE, A MEDICAL EMERGENCY...

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