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Iron Deficiency Anemia

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Iron Deficiency Anemia

Definition of Anemia

TABLE 1: The World Health Organization (WHO) definition of anemia.

Age	6 months to 5 years	5–11 years	12–14 years	15–19 years
Hemoglobin (g/dL)	<11	<11.5	<12	Girls: <12 Boys: <13

One often wonders if the definition of anemia is similar for Indian children as for the rest of the world. A large scale, nationally representative survey of children and adolescents aged 0–19 years was conducted in India (Comprehensive National Nutrition Survey) in 2019. Compared with the existing World Health Organization (WHO) cutoffs, the study cutoffs for hemoglobin (Hb) in healthy children were lower, usually by 1–2 g/dL. The findings support a reexamination of the WHO Hb cutoffs to define anemia (**Table 1**). However, these new findings have not yet been adopted for clinical use.

The prevalence of anemia has worsened in the country in recent years. The implementation of the anemia control program in the country has not been successful (**Table 2**).

TABLE 2: Prevalence of anemia (Hb < 11 g/dL) in children (6 months to 5 years), in selected states of India, as per the National Family Health Survey (NFHS).

State	NFHS-5 (2019–21)	NFHS-4 (2015–16)
India	67%	59%
Assam	68%	36%
Delhi	69%	60%
Karnataka	66%	61%
Maharashtra	69%	54%
Punjab	71%	57%
Rajasthan	72%	60%
Tamil Nadu	57%	51%
Uttar Pradesh	66%	63%
West Bengal	69%	54%

Reasons for the High Prevalence of Nutritional Anemia in India

- ☑ Excessive milk intake (milk consumption should not exceed 500–600 mL/day in children 1–5 years)
- ☑ Delayed introduction of complementary foods. For children older than 1 year, if still bottle-fed, discontinuation of the bottle will help to reduce milk intake and increase the intake of solid food
- ☑ The diet is predominantly carbohydrate (wheat and rice) based and vegetarian
- ☑ Worm infestation.

The most common age for the presentation of iron deficiency anemia (IDA) is 6 months to 2 years, and adolescence, due to increased iron requirements related to rapid growth.

Clinical and Subclinical Manifestations of Iron Deficiency (Anemia)

- ☑ Adverse effects on neurodevelopment, growth, and immunity
- ☑ Reduced exercise capacity and irritability
- ☑ Pica
- ☑ Breath-holding spells
- ☑ Febrile seizures
- ☑ Defects in leukocyte function
- ☑ Cerebral vein thrombosis (stroke).

Diagnosis of Iron Deficiency Anemia

- ☑ As IDA is widely prevalent in India, a therapeutic trial with oral iron is recommended in children suspected of iron deficiency.
- ☑ The diagnosis is confirmed if a trial of oral iron (3 mg/kg elemental iron per day) results in an Hb rise of >1 g/dL within 4 weeks for children with mild anemia or within 2 weeks for those with severe anemia.
- ☑ IDA can be reliably interpreted from an automated report, showing (1) low Hb, (2) low MCV, (3) reduced red blood cell (RBC) count, and often thrombocytosis. The peripheral smear has a microcytic hypochromic blood picture. Serum ferritin <12 µg/L and <15 µg/L in children aged 1–4 and ≥5 years, respectively, confirms iron deficiency.

Iron Supplementation: The Intensified National Iron Plus Initiative

- ☑ The Intensified National Iron Plus Initiative (I-NIPI) of the Ministry of Health and Family Welfare, Government of India, has ambitious and detailed recommendations for iron and folic acid supplementation throughout childhood.
- ☑ Every pediatrician should encourage and implement the recommendations of I-NIPI in everyday practice to reduce the burden of IDA in the community.
- ☑ It is to be emphasized that iron supplementation has to follow a lifecycle approach as it starts in infancy and continues into the end of adolescence for boys and into adulthood for girls. *Notably, all children, 6 months to 19 years, should receive regular iron supplementation.*
- ☑ The iron supplementation is continued till 45 years in women.
- ☑ The practice of delayed cord clamping is encouraged and recommended.

TABLE 3: Supplementation of iron + folic acid: The Intensified National Iron Plus Initiative.

Age	Frequency of administration of iron + folic acid	Preparation	Albendazole (tablet: 400 mg), twice a year
6 months to 5 years	Twice a week (fixed days)	1 mL IFA syrup = 20 mg elemental iron + 100 µg folic acid	1–2 years: ½ tablet ≥2 years: 1 tablet
5–10 years	Once a week	45 mg elemental iron + 400 µg folic acid	
10–19 years		100 mg elemental iron + 500 µg folic acid	

(IFA: iron and folic acid)

When should iron supplements be started in a term, breastfed baby?

As per I-NIPI: 6 months of age (**Table 3**). As per the American Academy of Pediatrics: 4 months of age. The authors recommend starting iron supplements at 4 months of age in term breastfed babies.

When should iron supplements be started in preterm babies?

At 2 weeks of age. Dose: Elemental iron: 2–4 mg/kg/day (maximum 15 mg).

Which is the best iron preparation?

Ferrous sulfate continues to be the gold standard and the preparation of choice. Syrup ferrous sulfate has the limitation of availability and shelf-life. Acceptable alternatives include ferrous fumarate, gluconate, or ascorbate. Colloidal iron and iron polymaltose complex have lower efficacy. Ensuring regular iron intake is more rewarding than protracted pondering over the best brand. The iron syrup is best given at the back of the mouth to avoid discoloration of teeth and gums, followed by rinsing the mouth with water.

- ☑ About 3 mg/kg/day of elemental iron, once daily, in the morning, or between meals, administered with water or juice is appropriate.
- ☑ The efficacy of once-daily administration is similar to three times/day. Milk or dairy products should be avoided for ~1 hour before and 2 hours after each dose to avoid limiting iron absorption.
- ☑ Iron is administered for 2 additional months after Hb is normal. As there are numerous iron preparations on the market, the pediatrician should check the product label for elemental iron content to avoid under- or overdosing.
- ☑ The strength of elemental iron can vary widely from 30 mg/15 mL to 100 mg/5 mL. Remember to continue iron supplements (prophylactic dose) as per the I-NIPI after treatment of IDA with daily iron is completed.

- ☑ Children with mild anemia ($\text{Hb} \geq 9 \text{ g/dL}$) should be reassessed by checking Hb or complete blood count ~4 weeks after treatment initiation.
- ☑ Children with moderate/severe anemia ($\text{Hb} < 9 \text{ g/dL}$) should be re-evaluated after 7–10 days to assess initial response to therapy, as demonstrated by improvement in well-being, reticulocytosis and increase in Hb.

Gastrointestinal Adverse Effects of Iron

Placebo-controlled trials have demonstrated that iron at 3 mg/kg/day rarely results in gastrointestinal (GI) symptoms (abdominal pain, constipation, and diarrhea). One may administer with food (but not milk), in divided doses, or on alternate days if iron indeed results in GI symptoms, which should be a rarity.

- ☑ Parenteral iron has a limited role in children. The response is not more rapid than oral iron.
- ☑ The indications include inflammatory bowel disease with blood loss, bowel resection, epidermolysis bullosa, heart failure, iron refractory IDA, and rarely poor tolerability to oral iron.
- ☑ The US Food and Drug Administration has approved the preparations of iron sucrose, ferric gluconate, and iron dextran in children. Ferric carboxymaltose is approved in the USA for children ≥ 1 year.

Iron deficiency anemia does not respond to oral iron: What to do?

- ☑ The common causes include poor compliance to iron, wrong formulation, or continuing excessive milk intake.
- ☑ Celiac disease should be considered and serology requested. Alternative diagnosis includes thalassemia minor and rarely iron-refractory IDA. Exclude GI blood loss (e.g., Meckel's diverticulum, polyps, and gastric ulcer) by requesting stool for occult blood.

Further Reading

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