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Review article:

Iron deficiency anaemia in paediatric age group: Review

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Abstract:
Almost 7 in 10 children aged 6-59 months are anemic, including 40 percent who are moderately anemic and 3 percent who are severely anemic. The prevalence of anemia does not vary by the sex of the child. Anemia is considerably higher in rural areas, among children of women with no education, and among children in households in the lower wealth quintiles. Children's anemia status is closely linked with the anemia status of the mother. Although state differentials in the prevalence of anemia are marked, a high prevalence of anemia is found in every state. This increase is largely due to a sharp increase in anemia among young children in rural areas; 90% of the cases being due to iron deficiency[1].The view was supported by an increasing prevalence of PH in communities moving from the hunter gatherer area to the agricultural societies depending mainly on maize which was deficient in absorbable iron. Present review article explains basic aspects concerning iron deficiency anemia in detail.
Keywords : Iron deficiency anemia , pediatric age

Introduction:

Almost 7 in 10 children aged 6-59 months are anemic, including 40 percent who are moderately anemic and 3 percent who are severely anemic. The prevalence of anemia does not vary by the sex of the child. Anemia is considerably higher in rural areas, among children of women with no education, and among children in households in the lower wealth quintiles. Children's anemia status is closely linked with the anemia status of the mother. Although state differentials in the prevalence of anemia are marked, a high prevalence of anemia is found in every state. The only states in which less than half of the children are anemic are Goa (38 percent), Manipur (41 percent), Mizoram (44 percent) and Kerala(45 percent).The prevalence of anemia among children 6-35 months has increased from 74 percent in National Family Health Survey (NFHS) 2 to 79 percent in NFHS-3. This increase is largely due to a sharp increase in anemia among young children in rural areas; 90% of the cases being due to iron deficiency[1].The view was supported by an increasing prevalence of PH in communities moving from the hunter gatherer area to the agricultural societies depending mainly on maize which was deficient in absorbable iron[2].

Historical aspects:

The clinical manifestations of iron-deficiency anemia may appear to have been recognized in earliest times. A disease characterized by pallor, dyspnea and edema was described in about 1500

B.C in the *Papyrus Ebers*, a manual of therapeutics believed to be the oldest complete manuscript extant[3]. The Greek mythological character, Iphiclus, supposedly drank iron rust dissolved in wine and was cured of impotence!! From the 16th through to the early 19th centuries, adolescent girls suffered a condition called chlorosis ('green sickness') that caused a greenish pallor associated with palpitations, breathlessness, ankle edema, thrombophlebitis and vague gastrointestinal complaints. Around 1830, scientists defined chlorosis as a disease of blood characterized by pale appearance and lack of iron. Pierre Blaud became famous by successfully treating affected individuals with a combination of ferrous sulfate and potassium carbonate. Between 1890 and 1920, the incidence of chlorosis decreased dramatically, not because of iron therapy, but because women stopped wearing tight-fitting corsets. Alchemists and physicians of the 16thcentury prescribed iron for medicinal use. Iron salts were given to young women to treat what was then described as chlorosis, an arcane term for anemia usually due to iron or protein deficiency.[5]

Iron was identified as a constituent of animal liver and blood in the early 18th century. In 1825, hemoglobin (Hb) content was determined to be 0.35%, a value extremely close to the Hb iron content of 0.347% calculated by modern methods. Between 1832 and 1843 chlorosis was defined by low levels of iron in the blood and reduced number of red cells. Boussingault first described the nutrition essentiality of iron in 1872. In 1895, Bunge accurately described anemia of chlorosis in terms of nutritional iron deficiency. One specific feature of iron deficiency, koilonychia comes from twentieth century description by Kanzelson (Davies-1931) although it is represented in the ancient 'Lydney hand.' Iron containing chalybeate (named after the Chalybes, skilled iron workers in Roman Asia Minor) waters has been recognized for their healing properties since prehistoric times. Bunge in (1902) in his pathological and physiological chemistry states that foods poor in iron leads to anemia. Hutchinson in 1923 reflected the views of many when he stated that 'iron contained in hemoglobin and its derivatives' is very ill observed[6]. Understanding of IDA by the early 1930s has been summarized by the Americans, Wintrobe and Beebe (1933). Her recommendation that iron should be given to non-breast fed infants from first months of life because this can support higher levels of hemoglobin later in infancy, stands good today[6].The specific consequences of iron deficiency with or without associated anemia, on immune responses and growth and cognitive function were still poorly defined. We also recognize that excessive dietary iron and inappropriate iron supplementation have adverse effects by initiating unwanted free radical activity[7].

Iron Metabolism:

Iron's importance in biochemistry lies in its ability to exist in two stable forms: the relatively inactive ferric (Fe^{3+}) and biochemically active ferrous (Fe^{2+}) state[8]. This property makes it an ideal atom to be involved in electron transfer, which forms the basis of many enzyme-controlled biochemical reactions. Iron is therefore not just important as heme iron to carry oxygen but is also essential to the working of many of the body's enzyme systems (Table 4.1).Approximately half the enzymes of Krebs cycles contain iron or require it

as a cofactor. Therefore, although most of the iron metabolized each day is used to synthesize hemoglobin, chronic iron deficiency may produce a wide variety of effects other than anemia.

Humans appear to be unique in their inability to excrete excess iron[9]. Iron loss (about 1-1.5 mg/day) is achieved almost exclusively in male by desquamation of skin and loss of mucosal cells from the gastro intestinal and urinary tracts[10]. In the female, iron is also lost through menstruation and during pregnancy. Iron loss by any of these means is relatively constant and cannot be altered in response to changes in body iron status. In the absence of a physiological mechanism for the excretion of excess iron, iron balance is achieved by control of iron absorption[11]

Iron absorption:

Three factors are important in determining the amount of iron absorbed from the diet: total iron content of the diet, bioavailability of the iron in the diet and control of iron absorption by the intestinal mucosal cells. Only the latter is responsive to body iron status and requirements.

Dietary iron content:

Total iron content is probably the single most important dietary factor in determining the amount of iron absorbed from the gut[12]. An adult male will absorb about 10% of this (0.5-1 mg/day). In iron deficiency, the amount of iron absorbed can be increased to a maximum of 3.5 mg/day[13]. Large amounts of dietary iron do not block iron absorption but as the amount in the diet increases, the percentage absorbed decreases. Different foodstuffs contain different proportions of iron; vegetarian diets are more likely to have inadequate iron content than mixed diets.

Foods and Drugs That Impair Iron Absorption

- Taking oral iron with food reduces absorption
- Caffeinated beverages (especially tea)
- Calcium containing foods and beverages
- Calcium supplements
- Antacids
- H-2 receptor blockers
- Proton pump inhibitors

Bioavailability of dietary iron

The bioavailability of dietary iron is also important in determining the amount of iron absorbed from the diet[14]. Dietary iron is in two forms: organic or heme iron derived from hemoglobin and myoglobin, and inorganic or non heme iron. There is a different absorptive pathway by which iron can enter the gut mucosal cells for each of the two types of dietary iron[15].Moreover the absorption of non heme-derived iron is reduced by the absence of heme iron, and the increased intake of phytates and phosphates further reduces the availability of absorbable iron. In contrast, human milk has low total iron content but the iron is in a form which is highly bioavailable[16] and which is also able to directly enhance the amount of iron absorbed from other foodstuffs in the early weaning diet[17].

Mucosal cell control

Gut mucosal cell control of iron absorption is not well defined but the amount of iron absorbed via the mucosa is responsive to body iron stores[18] and the erythropoietic activity of the bone marrow[19]. Increases in body iron lead to a reduction in iron absorbed from the gastrointestinal tract and when body iron stores are reduced, more iron is absorbed. Erythropoietic activity has the opposite effects: in conditions associated with high levels of erythropoietic activity, iron absorption is

increased but in disorders such as hypoplastic anemia where erythropoietic activity is reduced, iron absorption is reduced. The amount of dietary iron absorbed can be controlled at both phases of mucosal cell absorption.

Understanding of the mechanism of iron absorption has been made more difficult by the fact that the pathways for the absorption of inorganic iron and for heme are different. These pathways do seem to merge within the intestinal cell, however since the feeding of heme is not followed by the appearance of heme in the plasma (Fig 4.1). The existence of a heme receptor on intestinal cells has been described, but neither the putative receptor nor its function has been well characterized. The entry of iron into the intestinal cells has been studied by the use of pulse-chase experiments, and the existence of a pathway in which a β_3-integrin and a protein designated mobilferrin are involved in transporting iron into the cells. The partial amino acid sequence of the latter has been found to be that of calreticulin. These proteins are believed to form a complex that has been designated paraferritin (although it contains no ferritin) and which also contain the divalent metal tranporter-1 (DMT-1). Paraferritin appears to have ferrireductase activity. However another protein, duodenal cytochrome b (dcytb) reductase, which seems to reduce ferric iron to ferrous iron, has been characterized[20].

Assessment of body iron stores:

Detectable abnormalities occur in sequence as the magnitude of iron deficiency worsens (Table 4.2)[21]. The eventual changes in red cell morphology are nonspecific and occur late. Of more importance, and usually the first indication of iron deficiency are changes in the red cell indices. Most modern automated instruments measure red blood cells, hemoglobin, and mean corpuscular volume (MCV) directly. The direct measurement of MCV has made this a sensitive parameter of red cell changes and it has overtaken the more traditional measurements of mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH) as the primary indication of possible iron deficiency. Many modern blood counters produce two dimensional red cell maps that can often demonstrate the presence of iron-deficient red cells. No single confirmatory test is appropriate in all situations.

- S ferritin is a sensitive measurement of iron deficiency[21, 22] but is an “acute phase reactant” whose synthesis increases nonspecifically in response to inflammation, infection or malignancy. Liver cell damage also raises the S ferritin independently of body iron status.
- The increasing availability of radioimmunoassay of plasma TFR has provided a new method of diagnosing iron deficiency[23]. Plasma TFR concentration is proportional to marrow red cell turnover: erythroid hypoplasia (hypoplastic anemia, chronic renal failure) and erythroid hyperplasia (chronic hemolytic anemia)increases plasma TFR. TFR levels are also increased in iron deficiency and, in the absence of other conditions causing erythroid hyperplasia, plasma TFR is a sensitive indicator of iron deficiency[24] . Unlike S. Ferritin, plasma TFR is not affected by chronic inflammation or liver disease.

Although available for number of years, these methods have not been taken up by many hematology laboratories.

- In difficult cases, bone marrow examination after staining with Pearl's reagent will clarify the situation. In iron deficiency, neither the marrow macrophages nor erythroblasts contain iron. In the anemia of chronic disease there is plenty of iron present in the macrophages but none in the red cell precursors. Normally about 20% of erythroblasts contain iron (sideroblasts).

Iron requirements :

New born infants have approximately 75 mg/kg of body iron, 75% of which is in the form of hemoglobin. On an average, infants almost triple their blood volume during the 1st year of life and will require the absorption of 0.4-0.6 mg daily of iron during that time to maintain adequate stores[26].

Premature infants have a lower level of body iron at birth, approximately 64mg in infants weighing 1 kg. The loss of blood drawn for the lab test and the rapid rate of postnatal growth lead to higher requirement for dietary iron than in term infants- 2.0-2.5 mg/kg daily to prevent late anemia[27].

Assuming that 10% of that iron in a mixed diet is absorbed, the recommended iron intake is approximately 7 mg/day for term infants aged 5-12 months, 6 mg/day for toddlers 1-3 years and 8 mg/kg for children aged 4-12 years.

Iron deficiency :

Iron deficiency is the state in which the content of iron in the body is less than normal. It occurs in varying degrees of severity that merge imperceptibly into one another. *Iron depletion* is the earliest stage of iron deficiency in which storage iron is decreased or absent but serum iron concentration, transferrin saturation and blood hemoglobin levels are normal. *Iron deficiency without anemia* is a somewhat more advanced stage of iron deficiency, characterized by decreased or absent storage iron, usually low serum iron concentration and transferrin saturation, but without frank anemia. *Iron deficiency anemia* is the most advanced stage of iron deficiency. It is characterized by decreased or absent iron stores, low serum iron concentration, low transferrin saturation and low blood hemoglobin concentration.

Epidemiology:

The prevalence of iron deficiency anemia varies so much between age groups, between sexes, between economic groups and by geography that overall prevalence statistics are meaningless. Estimates are as many as 3/4th of the world population is iron deficient have been made but they are undoubtedly extravagant[28]. Table 4.3 provides some data regarding the prevalence in different populations around the world.

Etiology:

In children, as in adults, iron balance is related to the ratio of iron absorbed from the diet to the amount lost from the tissues by desquamation and bleeding. However in children other factors are also important, namely the total amount of iron present at the time of birth and the increased demand for iron for growth which is maximal in the first 6 months of life and during puberty. In the adult, the approach to determine the cause of iron deficiency is dominated by the search for blood loss. In the child especially below 3 years of age, evaluation of the causes of iron deficiency

requires an understanding of the developmental and dietary factors that affect the total body iron stores.

Developmental factors :

Fetus and Neonate :

The developing fetus is a little affected by maternal iron stores. Only in extreme maternal iron deficiency is any degree of anemia seen in the fetus[29]. In general, the fetus acts like a parasite, receiving maternal iron at the expense of the mother. In the vast majority of cases, babies of iron deficient mothers are born with normal hemoglobin concentrations. Infant serum iron and TIBC are also usually normal in the presence of maternal iron deficiency[30, 31, 32]. At the same time as being able to sequester iron from the mother into the fetus, the placenta also acts like a barrier excluding excess iron and preventing fetal iron overload. Consequently maternal iron supplementation doesn't influence fetal iron status[33]. A full term infant at birth is iron replete with an iron concentration of about 80 mg/kg body weight compared with 55 mg/kg body weight for an adult male[34]; 50 mg/kg is present as red blood cell iron, 25 mg/kg as storage iron and 5 mg/kg as myoglobin[35]. The extra iron is needed to cope with the additional requirements of the accelerated rate of growth that takes place in the first few months of life. Iron stores at birth may be almost completely independent of maternal iron status but they are dependent on two other factors: birth weight and neonatal red cell mass. Placental iron transport is insignificant until the 3rd trimester when iron transport increases dramatically to as much as 4 mg/day. Infants born before 26 weeks' gestation have very low iron stores; in those born in 3rd trimester, iron stores are proportional to birth weight. A 1kg preterm will have 50 mg of total body iron compared with the 320 mg of a 4kg full term baby. The effect of this reduction is accentuated by the greater relative growth potential of the 1 kg preterm infant.

Red cell mass is determined by hemoglobin concentration and red cell volume. Although red cell volume is more or less uniform at 80-90 ml/kg, Hb concentration at birth can vary from 13.5 to 21 g/dl in normal infants. The timing of umbilical cord clamping influences birth Hb concentration. At delivery, two-thirds of the red cells in the fetal circulation are in the infant and one-third in the placenta and cord. In the 3minutes immediately following birth, uterine concentrations will increase the amount of blood cells in the fetus to> 85% so early clamping of the cord can reduce the infant's iron content by between 15 and 30%[36].

Infancy :

During the first few weeks of life, erythropoiesis almost stops as the infant's red call mass drops to a level appropriate for the oxygen rich extra-uterine environment[37]. Iron is stored until erythropoiesis resumes, usually when the infant's Hb has dropped to 11-12 g/dl[38]. In the normal term infant, the iron stored during this time is adequate to cope with the expected doubling of body weight that takes place in the first 5 months of life. After this time, iron absorption from the diet becomes critical to maintenance of normal iron balance. It has been estimated that a term infant needs 100 mg of iron in the first year of life from the diet to maintain the Hb level of 11 g/dl but a preterm infant may require two to four times as much[39]. As stated above, newly born

infants are iron replete. This is reflected by laboratory findings. Cord blood iron levels are high at 150-220 µg/dl, dropping to 130 µg/dl after 24 hours. Following resumption of erythropoiesis at 8 weeks, iron levels drop further to 80 µg/dl[40].Serum Ferritin is also raised at birth with levels between 100 and 200 µg/L; it then increases further over the first 8 weeks of life but then begins to drop following resumption of eruthropoiesis[41]. At 1 year, the mean Serum Ferritin is usually 30 µg/L. Serum TF levels are proportional to gestational age. This is a developmental phenomenon and, at least in the preterm infant, is not related to iron status[17].

Early childhood :

During childhood, total body iron increases in proportion to body weight. After 6 months of age, growth slows and diet becomes varied. As long as the diet has an adequate iron content, iron deficiency anemia is unusual. Even so, measured parameters of serum iron and TF saturation remain persistently low. TF saturation of 10% are not uncommon during early childhood but despite this erythropoiesis continues satisfactorily. Serum Ferritin also remains low but levels < 10 µg/L indicates depletion of iron stores.

II **Dietary factors :**

The importance of dietary factors and the bioavailability of iron containing foods are very important factors. These dietary factors are particularly important to the development of iron deficiency in early childhood. Human breast milk has low total content of iron but like heme iron, the iron present in breast milk is highly bioavailable and able to enhance the amount of iron absorbed from other foodstuffs in early weaning diet[18]. Cow's milk, on the other hand, has low content of poorly bioavailable iron and its high phosphate content interferes with the absorption of iron from other foods. Cow's milk will be associated with increased intestinal blood loss[42]. Thus, despite having an apparently low total iron intake, the breast-fed infant is relatively protected from iron deficiency in early childhood compared with the child with a high intake of cow's milk.

Pallor is one of the presentations of anemia, but this is clinically significant only in moderate and severe anemia.

- Decreased work performance: Objective measurements of work performance and studies using O_2 consumption show severe iron deficiency (Hb< 8 g/dl) and mild iron deficiency (Hb between 8 and 12 g/dl) lead to decreased work performance as estimated by VO_2max measurements.
- PICA: The craving to eat unusual substances such as dirt, clay, ice, laundry starch, salt, cardboard, or hair is a classic manifestation of iron deficiency and is usually cured promptly by iron therapy.
- HEADACHE: Iron-deficient patients frequently complain of headache, but headache is a common symptom, and the data that have been presented are all anecdotal.
- Paresthesia and Other Neurologic Symptoms: Breath holding spells have been attributed to iron deficiency. Anecdotal reports of intracranial hypertension with papilledema are buttressed by apparent response to iron therapy. Stroke in children has been

associated with IDA.

- Oral and Nasopharyngeal Symptoms: Burning sensation of tongue and dysphagia has been proposed as cause of atrophic rhinitis.
- Dysphagia: In the laryngopharynx, mucosal atrophy may lead to web formation in the post cricoid region, thereby giving rise to dysphagia (Patterson-Kelly/Plummer-Vinson syndrome). Abnormal motility of the esophagus has also been documented in the iron- deficient patients.
- Restless legs: Restless legs are a common nocturnal problem, especially in the elderly, and has been associated with iron deficiency.
- Hair loss
- Long-standing, severe iron deficiency affects the cells that generate the finger nails producing koilonychias.
- In infants, iron deficiency is associated with poor attention span, poor response to sensory stimuli, and retarded behavioral and developmental achievement, even in the absence of anemia.

Although a considerable number of studies with a positive outcome have been reported, many of these have been criticized because of the lack of controls, and the possibility that socio economic factors may have a confounding effect.

DIAGNOSIS:

1. BLOOD

A- Hemoglobin: hemoglobin is below the acceptable level for age. In the present study 11g/dl was the cut off to consider anemia.

Age and Sex group	Hemoglobin values (in g/dL)				
	Non Anemic	**Anemic**	**Mild anemia**	**Moderate anemia**	**Severe anemia**
Children 6-59 Months	11.0 or more	< 11.0	10-10.99	7-9.99	<7
Children 6-11 years	11.6 or more	<11.6	10-11.49	7-9.99	<7
Children 12- 14 years	12.0 or more	< 12.0	10-11.99	7-9.99	<7
Non-pregnant women	12.0 or more	< 12.0	10-11.99	7-9.99	<7
Pregnant Women	11.0 or more	< 11.0	10-10.99	7-9.99	<7
Men	13.0 or more	< 13.0	10.-12.99	7-9.99	<7

[Source : WHO/UNICEF/UNU 2001(4)]

B- Red cell indices: Lower than normal MCV, MCH, and MCHC for age. Widened red cell distribution width (RDW) in association with a low MCV is one of the best screening tests for iron deficiency anemia. The RDW is high (>14.5%) in iron deficiency anemia and normal in thalassemia (<13%).

The reference value of red cell indices in our lab are as shown in the table below.

Age in yrs.	Haematocrit (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)
1-2	34 ± 4	78 ± 6	27 ± 2	34 ± 2
2-6	37 ± 3	81 ± 6	27 ± 3	34 ± 3
6-12	40 ± 5	86 ± 9	29 ± 3	34 + 3

C-

Blood smear: Red cells are hypochromic and microcytic with anisocytosis and poikilocytosis, generally occurring only when hemoglobin level falls below 10 g/dl. Basophilic stippling can also be present but not as frequently as present in thalassemia trait.

D- Reticulocyte count: it is usually normal; however, in severe iron deficiency anemia associated with bleeding, the reticulocyte count of 3-4 % may occur.

E- Platelet count: the platelet count varies from thrombocytopenia to thomobocytosis. Thrombocytopenia is more common in severe iron deficiency anemia; thrombocytosis is present when there is associated bleeding from the gut.

F- Free erythrocyte protoporphyrin: the incorporation of iron into protoporphyrin represents the ultimate stage in biosynthetic pathway of heme. Failure of iron supply will result in an accumulation of free protoporphyrin not incorporated into heme synthesis in the normoblast and the release of erythrocytes into the circulation with high free erythrocyte protoporphyrin level.

a- The normal FEP level is 15.5 ± 8.3 mg//dl. The upper limit of normal is 40 mg/dl.

b- In both iron deficiency and lead poisoning, the FEP level is raised. It is much higher in lead poisoning than in iron deficiency. The FEP is normal in α and β thalassemia minor. FEP elevation occurs as soon as the body stores of iron are depleted, before microcytic anemia develops. An elevated FEP level, therefore, is an indication for iron therapy even when anemia and microcytosis have not yet developed.

G- Serum ferritin: the level of ferritin reflects the level of body iron stores; it is quantitative, reproducible, specific, and sensitive and requires only a small blood sample. A concentration of less than 12mg/ml was considered diagnostic of iron deficiency in present study. Normal ferritin levels can exist in iron deficiency when bacterial or parasitic infections, malignancy, or chronic inflammatory conditions coexist because ferritin is an acute phase reactant.

H- Serum iron and iron saturation percentage: serum iron estimation (60-170 µg/dl was taken as normal range in present study) as a measure of iron

deficiency has serious limitations. It reflects the balance between several factors, including iron absorbed, iron used for hemoglobin synthesis, iron released by red cell destruction, and the size of iron stores. The serum iron concentration represents equilibrium between the iron entering and leaving the circulation. The serum iron has a wide range of normal, varies significantly with age, and is subject to marked circadian changes (as much as 100 µg/dl during the day). The limitations:

1. Wide normal variations(age, sex, laboratory methodology)
2. Time consuming
3. Subject to error from iron ingestion
4. Diurnal variation
5. Falls in mild or transient infection.

Serum transferrin saturation >16% is taken as normal for all age groups.

I- Increased iron binding capacity: in the present study the normal range used was around 350 µg/dl.

J- Therapeutic trial: The most reliable criterion of iron deficiency anemia is the hemoglobin response to an adequate therapeutic trial of oral iron. A reitculocytosis with a peak occurring between the 5th and 10th day followed by a significant rise in hemoglobin level occurs. The absence of these changes implies that iron deficiency is not the cause of the anemia. Iron therapy should then be discontinued and further diagnostic studies implemented.

Other tests for iron deficiency not in common usage include the following:

A- Serum transferrin receptor level (STfR): This is a sensitive measure of iron deficiency and correlates with hemoglobin and other laboratory parameters of iron status. The STfR is increased in instances of hyperplasia of erythroid precursors such as IDA and thalassemia and is normal in chronic inflammations. It is therefore of great value in distinguishing iron deficiency from the anemia of chronic disease. It can be measured by sensitive ELISA technique.

B- Red blood cell zinc protophorphyrin/heme ratio: when available bone marrow iron is insufficient to support heme synthesis, zinc substitutes for iron in protoporphyrin IX, and the concentration of zinc protoporphyrin relative to heme increases. This test is more sensitive than plasma ferritin level tests, is inexpensive and simple, and is not altered in chronic inflammatory diseases or acute infections.

C- Bone marrow

a- Delayed cytoplasmic maturation

b- Decreased or absent stainable iron.

TREATMENT :

A- Nutritional counseling

1- Maintain breast feeding for at least 6 months, if possible.

2- Use iron fortified cereal from 6months to 1 year.

3- Use evaporated milk or soy-based formula when iron deficiency is due to hypersensitivity to cow milk.

4- Provide supplemental iron for low birth weight infants:

a- Infants 1.5-2.0 kg: 2mg/kg/day supplemental iron.

b- Infants 1.0-1.5 kg: 3mg/kg/day supplemental iron.

c- Infants <1 kg: 4 mg/kg/day supplemental iron.

5- Facilitators of iron absorptions such as vitamin c rich foods (citrus, tomatoes, and potatoes), meat, fish, and poultry should be included in the diet; inhibitors of iron absorption such as tea, phosphates and phytates common in vegetarian diets should be eliminated.

B- Iron therapy

Oral iron:

Elemental iron should be prescribed in a dose of 3 mg/kg up to a daily maximum of 180 mg usually given as two divided doses. To avoid accidental iron over dosage, parents of guardians should be warned of the dangers of medicinal iron and all preparations should be kept in child proof containers and out of reach of young children. The following preparations provide 3mg of iron:

- 15 mg of ferrous sulphate
- 9 mg of ferrous fumerate
- 26 mg of ferrous gluconate
- 9 mg of ferrous succinate
- 17 mg of ferrous glycine sulfate
- 21 mg of sodium iron edentate

Table-1: Percentage and amount of iron in some commonly used oral iron preparations[5, 14]

Preparation	Iron compound (mg/tab)	Elemental iron mg/tab (%)
Fe-sulfate(hydrous)	300	60 (20%)
Fe-sulfate(dried)	200	65 (32.5%)
Fe-fumarate	200	66 (33%)
Fe-gluconate	300	36 (12%)
Fe-succinate	100	35 (35%)
Fe-bisglycinate	300	60 (20%)
Carbonyl iron	100	98 (98%)
Na-feredetate	231	33 (14%)

Parenteral iron:

Parenteral iron preparations are rarely indicated for the treatment of childhood and must only be considered if the diagnosis of the iron deficiency is absolutely certain.

The indications for parenteral iron preparations are:

- Demonstrated intolerance to oral preparations
- Where there is a need to deliver iron rapidly to iron stores
- In active inflammatory bowel disease where there is intolerance to oral iron.
- Where there is demonstrated patient non-compliance with oral iron with definite diagnosis or iron deficiency
- Where follow up of patient is impossible.

DOSAGE:

Only the intramuscular preparations containing the iron, sorbitol, and citric acid is licensed for use in children above 3 kg in weight. The majority of children in iron deficiency anemia are toddlers with inadequate diets. These children can be managed in the primary care setting in collaboration with the local hematological laboratory. However, all other children with iron deficiency need to be assessed in the hospital setting, where the full diagnostic facilities required are readily available. All cases without an obvious cause for the iron deficiency and those who fail to respond as expected to therapy should be referred to a pediatric hematologist.

C-Blood transfusions: A packed cell transfusion should be given in severe anemia requiring correction more rapidly than is possible with oral iron or parenteral iron or because of the presence of certain complicating factors. This should be reserved for debilitated children with infections, especially when signs of cardiac dysfunction are present and the hemoglobin level is 4 g/dl or less.

D- Partial exchange transfusion: A partial exchange transfusion has been recommended in the management of a severely anemic child under two circumstances:

1. In surgical emergency, when final haemoglobin of 9-10g/dl should attain to permit safe anaesthesia.
2. When anemia is associated with congestive heart failure, in which case is sufficient to raise the haemoglobin to 4-5g/dl to correct the immediate anoxia.

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