**DZIEWIERZ, Anna, DZIEWIERZ, Paulina, PIETRUSIŃSKA, Patrycja, SADOWSKA, Aleksandra, WELKIER, Aleksandra, SOBIŃSKI, Adam, MIŚKIEWICZ, Joanna, DUDEK, Aleksandra, MODER, Jakub, KWAŚNIEWSKA, Paula and ŚLIWA- TYTKO, Patrycja. Iron deficiency in children - causes, consequences, treatment - review of the literature. Journal of Education, Health and Sport. 2025;80:59534 eISSN 2391-8306.**
**https://doi.org/10.12775/JEHS.2025.80.59534**
**https://apcz.umk.pl/JEHS/article/view/59534**

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 17.03.2025. Revised: 09.04.2025. Accepted: 24.04.2025. Published: 28.04.2025.

# Iron deficiency in children - causes, consequences, treatment - review of the literature

**Authors:**

**Anna Dziewierz [AD]**

Mazowieckie Centrum Stomatologii Sp. z o.o. ul. Nowy Zjazd 1, 00-301 Warsaw

https://orcid.org/0009-0006-5632-0427

anna.dziewierz98@gmail.com

**Paulina Dziewierz [PD]**

Wroclaw Medical University, wyb. Ludwika Pasteura 1, 50-367 Wrocław

https://orcid.org/0009-0004-3132-2587

dzpaulina2@gmail.com

**Patrycja Pietrusińska [PP]**

The Silesian Academy of Medical Sciences Mickiewicza 29 str. 40-085 Katowice

https://orcid.org/0009-0008-0722-4396

pietrusinskapatrycja@gmail.com

**Aleksandra Sadowska [AS]**
J. Mikulicz-Radecki University Clinical Hospital in Wrocław: Wrocław, PL Borowska 213, 50-556 Wrocław
https://orcid.org/0009-0006-6458-1264
a.sadowska006@gmail.com

**Aleksandra Welkier [AW]**
Corten Dental Sp. z o.o. ul. Cybernetyki 19B 02-677 Warsaw
https://orcid.org/0000-0003-3552-6726
a.piasecka99@wp.pl

**Adam Sobiński [AS]**
MEDAR Private Healthcare Facility in Leczyca: Leczyca, PL Kilinskiego 4, 99 - 100 Leczyca
https://orcid.org/0009-0003-3063-5621
a.sobiński25@gmail.com

**Joanna Miśkiewicz [JM]**
Wojewódzki Szpital Zespolony w Kielcach, ul. Grunwaldzka 45, 25-736 Kielce, Poland
https://orcid.org/0009-0002-3300-940X
miskiewiczj10@gmail.com

**Aleksandra Dudek [AD]**
Jan Biziel University Hospital No.2 in Bydgoszcz, ul. Kornela Ujejskiego 75, 85-168 Bydgoszcz, PL
https://orcid.org/0009-0000-2547-3574
aleksandra.d2501@gmail.com

**Jakub Moder [JM]**
Warsaw Southern Hospital, 99 Rotmistrza Witolda Pileckiego St., 02-781 Warsaw
https://orcid.org/0009-0006-7747-6623
jmoder42@gmail.com

**Paula Kwaśniewska [PK]**
Szpakmed Kochłowice ul. Radoszowska 163, 41-707 Ruda Śląska
https://orcid.org/0009-0007-2576-7573
kwasniewska.paula@gmail.com

**Patrycja Śliwa-Tytko [PS]**
Medical University of Lublin: Lublin, Poland, PL Aleje Racławickie 1, 20-059 Lublin
https://orcid.org/0009-0005-5417-4924
sliwa.pat@gmail.com

**Abstract**

Iron deficiency (ID) is one of the most widespread nutritional deficiencies. Children belong to one of the high-risk groups for iron insufficiency, due to the increased requirement during the period of intensive growth. ID can have unfavorable effects on brain development and the ability to learn. It can also impair the development of cognitive functions in children. Iron deficiency occurs as a result of insufficient iron intake from the diet, malabsorption associated with gastrointestinal diseases, increased requirement e.g. due to frequent bleeding. Iron is present in food in two forms: haem and non-haem. The haem form is found in animal products and is better absorbed. Early detection is essential to prevent the effects of insufficiency. The most frequently used test to diagnose iron deficiency is the ferritin level. However, a complete blood count is recommended to determine the overall condition of the body. When ID impairs the function of red blood cells, anaemia occurs. To prevent iron deficiency, women should be taken care of during pregnancy by introducing appropriate supplementation. Nutrition plans that incorporate iron-fortified foods in high-risk ID areas are also becoming more prevalent. Treatment of the insufficiency involves supplementation by oral or intravenous administration or through blood transfusions. In each method, a well-balanced diet containing foods rich in highly absorbable forms of iron is essential.

**Key words:** iron deficiency, iron, child development, iron metabolism

## Introduction

The WHO estimates that iron deficiency affects nearly 2 billion people worldwide and that 40% of children aged six months to five years have anaemia. Iron plays a significant role in the human body. It is involved in oxygen transport, cellular energy metabolism, DNA synthesis and cell proliferation. It is also essential for the development of the nervous system, normal growth and the formation of the body's immunity. This article summarizes current knowledge on iron deficiency with consideration of its impact on physical and psychological child development. The work also focuses on methods to prevent and treat this insufficiency.

## Methodology

The literature review was based on articles found in PubMed and Google Scholar databases. In preparing for this review, database searches using the terms “iron deficiency”, “iron deficiency anemia”, ‘’iron metabolism” and ‘’iron and child development’’ were performed. The date range was focused on papers 2015 and later. Only articles published in the English-language literature were considered in the search for information for the article.

## Iron metabolism and it is role in the organism

Iron is a key micronutrient at every stage of human life. In children, it has a special role due to the rapid growth and development of all systems. [1] Excessive iron deficiency induces cells death, confirming the great importance of this element in fundamental biological processes. [2] This metal permits a number of cellular processes to occur, such as DNA synthesis and repair, energy production in the mitochondria during cellular respiration, the cellular life cycle, cell signaling and host defense. [3,4] Iron is required for the proper functioning of enzymes that are involved in about 180 biochemical reactions in the body. These include cytochrome oxidase, cytochrome c, α-glycorophosphate oxidase, succinic dehydrogenase and aconitase. [5] In addition, iron incorporated into haem is a major component of haemoglobin (Hb) and myoglobin (Mb). It is involved in the transport and delivery of oxygen by erythrocytes and the storage of oxygen in muscles. [4] In brain cells, it is participating in the production of neurotransmitters and in the process of myelination. [6] Iron is furthermore essential for the synthesis and proper functioning of thyroid hormones. [7]

The widespread presence of iron in the body's cells is the reason that deficiency of this element gives a variety of symptoms from a number of systems. [5]

The majority of body iron (80%) is found in erythrocyte haemoglobin, with the remainder present in macrophages, hepatocytes, haem-containing proteins like mioglobine, iron-sulphur cluster-containing (ISC) proteins and non-haem proteins.[2] Iron exhibits a strong redox activity, i.e. the ability to donate and accept electrons. In the body, it exists in two forms: $Fe^{2+}$ and $Fe^{3+}$. The dicationic form can be toxic in certain situations. $Fe^{2+}$ reacts with hydrogen peroxide ($H_2O_2$) to produce a hydroxyl radical (ROS), which is oxidized to $Fe^{3+}$ (Fenton reaction). The course of the reaction is dependent on the pH of the environment. An example of the toxic action of the hydroxyl radical is to attack cellular lipids and trigger the lipid peroxidation cascade, leading to cell damage and death. ROS also harms proteins, nucleic acids and carbohydrates. Its influence is potentially mutagenic and carcinogenic. [4]

Iron homeostasis is strictly regulated. As explained above, excess iron is toxic and therefore its availability in the body is subject to complex regulatory processes at the systemic and cellular levels. [3,8] In humans, there is no mechanism to excrete excess iron, so its balance is attained by controlling iron absorption in the intestine and mobilization from the liver and macrophages. [9] Transferrin is the protein responsible for the transport of iron in the blood. [8] Stored iron is in the macrophages of the spleen, bone marrow or liver.[9]

In adults, iron absorption from the gastrointestinal tract is limited to 1-2 mg per day. Most of the iron (approximately 25 mg) is recovered by recycling of ageing erythrocytes. The spleen is the organ that filters red blood cells. Macrophages present in the spleen have the capacity to distinguish ageing erythrocytes from healthy cells and selectively phagocytise them. In infants and children, the requirement for iron to produce erythrocytes and new muscle cells is higher, so up to 30% of this element comes from the diet. [1]

The protein that mainly regulates iron haemostasis is hepcidin. Hepcidin is a peptide hormone synthesised essentially in the liver. [10] When hepcidin levels increase iron is retained in enterocytes or macrophages and is not available for metabolism. When hepcidin levels decrease, iron is released into the circulation. [9] Hepcidin expression also increases in the presence of inflammation or infection. [10]

**Dietary sources of iron**

In food, iron occurs in two forms. The first comes only from animal products - the haem form - and the second is found mainly in plant products - the non-haem form. [8] Iron absorption is influenced by the type of chemical form of iron consumed, the body's requirement for this element and the presence of absorption modifiers. Haem iron is better absorbed (15-40%), while non-haem iron is only absorbed in a small percentage (1-15%). [11]

Iron absorption occurs mainly in the duodenum and upper part of the jejunum. In order for iron to be absorbed, it must exist in the ferrous state ($Fe^{2+}$) or be bound to a protein such as heme [12]. To maximize absorption, iron in the $Fe^{3+}$ form (non-haem form) is reduced to $Fe^{2+}$ (haem form) by gastric acid, the enzyme ferric reductase and ascorbic acid from the diet. The first absorption pathway involves haem iron. The protein involved in this process is the intestinal haem iron transporter (HCP1), which is located on the surface of enterocytes [8]. It transports iron directly into the intestinal cell. The iron is then released into the plasma with the involvement of the haem exporter FLVCR1 or is converted to $Fe^{2+}$. The second absorption pathway involves reduced non-haem iron. Divalent metal transporter 1 (DMT1) transports $Fe^{2+}$ into the enterocyte. Ferritin transports it through the cytoplasm or stores part of it, and ferropoietin allows it to exit the cell into the blood. As it passes through the membrane, non-haem iron returns to its original $Fe^{3+}$ form with the involvement of hephaestin or ceruloplasmin. [13]

Non-heme iron accounts for up to 90% of the iron consumed from food, but in addition to its low absorption rate, it is also characterised by susceptibility to modifiers. [14] These can be activators or inhibitors of absorption, so the appropriate composition of the diet is an important factor influencing the bioavailability of non-haem iron. [15] Factors that increase iron absorption include ascorbic acid, animal tissues (especially muscle and liver). Inhibitors include polyphenolic compounds, phytates, calcium. [14]

Unmodified cow's milk has a low iron concentration and contains calcium which has the potential to reduce the absorption of iron from other products. Calcium is a unique inhibitor, because it can also decrease the absorption of the haem form. For this reason, the latest recommendations state to limit the daily intake of milk in children to 500 ml. [16]

Polyphenols are potent inhibitors of iron absorption and can be found in plant sources including tea, wine and coffee. The study performed in United Kingdom highlights that global tea consumption is very high and may have an impact on the development of deficiency. The article shows that consumption of a test meal with tea is characterized by lower iron absorption compared to when the test meal was sipped with water. However, waiting an interval of as little as 1 h between eating and drinking tea has a significant effect in counteracting this inhibitory effect. [17]

Bioactivity of iron from food also depends on the physiological requirement of the body for this microelement. In cases of iron deficiency, iron absorption from food may be increased. [9] Products rich in iron are animal livers, chicken egg yolk, fish, meat, dried legumes and bran.[11] The table shows examples of products and their iron content. [18]

| **Products** | **Measure** | **Iron (mg)** |
|---|---|---|
| Beans, pink, mature seeds, raw | 1 cup | 14,22 |
| Corn flour, yellow, masa, enriched | 1 cup | 9,69 |
| Seeds, pumpkin and squash seed kernels, roasted, | 1 cup | 9,52 |
| Mollusks, oyster, eastern, wild, cooked, moist heat | 3 oz | 7,83 |
| Nuts, hazelnuts or filberts | 1 cup | 5,41 |
| Sausage, turkey, hot, smoked | 2 oz | 5,38 |
| Liverwurst spread | 0,25 cups | 4,87 |

Table 1. *Examples of iron content in food products based on data from the USDA National Nutrient Database for Standard Reference Legacy (2018) [18]*

**Iron deficiency in children**

Iron deficiency (ID) is a health-related condition in which the iron supply is too low to meet the body's needs and guarantee correct physiological processes. It can occur with or without anaemia. The indicator most used to assess iron metabolism in children is ferritin, whose serum concentration < 15 μg/L, demonstrates depletion of iron stores. [19]
Iron deficiency anaemia (IDA) occurs when iron deficiency impairs erythropoiesis. It is defined when haemoglobin (Hb) levels fall two standard deviations or more below the average for a healthy group. Standards are set for age and gender, respectively. [20]

Iron deficiency is the most common nutritional disorder worldwide. The problem is exacerbated in developing countries. ID is most often caused by insufficient iron supply. However, it can also be a result of problems with iron absorption in the gastrointestinal tract or excessive loss of this element from the body, e.g. during bleeding. [21]

The study conducted in Romania aimed to find the causes of iron deficiency in infants 6-12 months and in children 1-3 years. The number of children examined was 142 and the observations lasted more than 7 years. The study and control group included the same number of participants. As one of the conclusions, it was hypothesized that cow's milk consumption was the most common cause of iron deficiency anaemia. Among the study group, 67% of the anaemic children drank cow's milk; in the control group, this figure was only 17%.[22]

In normal birth weight infants with sufficient reserves at birth and no ID risk factors, iron requirements are low. Breast milk, which has a high bioavailability of iron (~50%) is sufficient to meet this requirement for the first 4-6 months of life. [23] With the beginning of the newborn's growth period around 6 months of age, tissue growth accelerates, and blood volume rises. The need for iron increases significantly. This is a period of risk for ID. [15] Iron is essential for many growth processes, but nervous system development is particularly vulnerable. Current research shows that inadequate iron supply between 6 and 24 months of age is associated with poorer outcomes in cognitive and neurobiological development. [24] In older children, ID also affects growth and development, but iron supplementation has an effect in this group [15]

There are also emerging studies showing that disruption of iron status during infancy and childhood causes changes in the nervous system that may persist into adulthood despite supplementation of the deficiency. Persistent deficits in learning, memory, speed of information processing, attention and increased risk of depression, anxiety or psychiatric disorders are observed. [24]

**Iron deficiency diagnostics**

Detection of iron abnormalities requires laboratory tests. Modern analytical methods make it possible to diagnose iron deficiency in the body at an early stage, even before the onset of symptoms. [25] The American Academy of Pediatrics recommends screening testing haemoglobin levels in every child at 12 months of age. [26] However, other studies and recommendations including the WHO argue that early identification of risk factors for iron deficiency is more important in paediatrics than routine laboratory testing. [27] Risk factors for

ID include prematurity and/or low birth weight, children from multiple pregnancies, children of mothers who developed anaemia during pregnancy, slow growth, feeding problems, insufficient dietary iron intake, high intake of unmodified cow's milk and low socioeconomic status [25, 27].

A complete blood count (CBC) and assessment of iron parameters is recommended as soon as risk determinant or the first worrying symptoms appear [27]. A single test is not sufficient to assess iron metabolism. It is important to comprehensively evaluate the results of the morphology and iron parameters and relate them to the individual patient's situation. [20] The most specific and sensitive test to assess iron deficiency is serum ferritin (SF). Its decrease reflects low iron stores in the body. According to the actual 2020 recommendations. WHO, a SF level of <12 µg/l in children younger than 5 years old and <15 µg/l in children older than 5 years old signals ID. [28] As the deficiency progresses, transferrin synthesis increases, and transferrin saturation saturation decreases. [29] The study also evaluates serum iron, the amount of which is low in ID, but its level fluctuates widely from day to day, so it is not a critical paramtter.[30] To confirm anaemia, red cell parameters should be assessed.[29] Anemia is diagnosed with a decreased red blood cell count and reduced hemoglobin concentration. According to the World Health Organization, the average Hb value in children aged 6-59 months in Poland is a range: 11.3-12.5 g/dl - an average of 12 g/dl (2019 data). [28] In IDA, erythrocytes are microcytic and hypochromic, as evidenced by low mean cell volume (MCV) and mean hemoglobin per cell (MCH) and increased red blood cell distribution width (RDW). [30] Iron deficiency anemia is categorized as microcytic hypochromic anaemia.[31] The introduction of new and more precise parameters to test iron metabolism is being tested in diagnostics. These are soluble transferrin receptor (sTfR) or hepcidin. Currently, these are only used in research. [32]

In summary, in the diagnosis of iron deficiency anemia, the following parameters from the blood test are most often evaluated: hemoglobin (Hb) [↓], serum ferritin [↓], transferrin saturation [↓], MCH, [↓] and MCV [↓]. [33] To avoid false-positive results, all tests should be performed in the absence of inflammation or infection.[20]

| Age | Hemoglobin [g/dL] | Ferritin [µg/L] | MCV [fL] |
|---|---|---|---|
| 0- 7 days | 13.5 - 20 | 153-1092 | 95-115 |
| 8-30 days | 10 - 16 | 247-692 | 85-100 |
| 1-3 months | 9.5 - 14.5 | 148-744 | 85-100 |
| 4-9 months | 9.5 - 13.5 | 21-240 | 75-95 |
| 9-24 months | 10.5 - 13.5 | 10-168 | 75-95 |
| 2-16 years | 11.5 - 15 | 10-99 | 77-85 |
| >16 years, girls | 12-16 | 18-103 | 78-95 |
| >16 years, boys | 13-17 | 16-213 | 78-95 |

Table 2. *Normal haemoglobin concentration, ferritin concentration and mean corpuscular volume (MCV) in children. [25]*

**Effects of iron deficiency**

Iron deficiency develops slowly, reducing the body's iron stores, initially presenting no symptoms (phase I) The progressive lack of this micronutrient starts to affect the production of red blood cells in the bone marrow (phase II) and other body systems impairing their function. When the parameters of erythrocytes are disturbed and hemoglobin drops, anemia appears (phase III). [34] Physiological oxygen requirements are not adequately met for all tissues.

The first symptoms of iron deficiency are pallor, fatigue, exercise intolerance, a feeling of shortness of breath, and fainting. [35] Headaches, sleep disturbances and impaired memory are also present. Dermatological problems appear such as dry skin, hair loss, itching, inflammation of the corners of the mouth [36, 37].

Pica is also described in the literature as a symptom of ID. It is a disorder characterized by the consumption of non-nutritious and inedible substances for a minimum of 1 month. The group of products includes chalk, soil, ice, uncooked rice, eggshells, paper and others. The exact name of the disorder depends on the name of the substance consumed.[38] The authors debate whether pica is only a symptom or a cause of iron deficiency. However, they agree that treatment of ID by oral or intravenous therapy results in a reduction or elimination of pica. [39] Iron deficiency during growth and development in children negatively affects many body systems, especially the brain, skeletal muscles, heart, digestive system and immune system. [40] Iron also has an important role in brain development and function. In children, its deficiency carries a risk of neurodevelopmental, behavioral and psychomotor disorders. ID is also

associated with reduced visual and auditory function. [41] The impact on the type and severity of these dysfunctions depends on the developmental period during which the brain was exposed to the deficiency. [42] The widely considered most important period for brain development is the first 1,000 days of life, from conception to about the age of two. [43] The most characterized changes in the brain relate to the effects of ID on the developing hippocampus, striatal body and certain neurotransmitters such as dopamine, serotonin, norepinephrine. The hippocampus belongs to the limbic system and is responsible for memory and spatial orientation. The striatal body is involved in the control of motor and executive functions, and neurotransmitters regulate brain function and behavioral and developmental behaviors. [44] Iron deficiency can lead to permanent disorders of behavior, learning and mental abilities. It results in reduced school achievements, concentration, and motor coordination. It is a risk factor for attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). [45] Changes in brain structures also cause dysfunction in children's emotion regulation systems, which can manifest as delayed emotional response or flat affect. This can influence the disruption of family and social relationships in children. [46]

A group of children were observed in Canada to examine the impact of iron deficiency on cognitive function. Participants aged 12-40 months were finally divided into two groups: chronic iron deficiency and iron sufficiency (IS). A. Gingoyon et al. used the Early Learning Composite (ELC), which assesses four cognitive skills (isual reception, fine motor, receptive language, expressive language). When tested at 4 months, the iron-deficient children's scores were on average 6.4 points lower than the control group. After 12 months, the difference was 7.4 points. Differences in ELC continued throughout the observation despite comparable iron and feritin levels in both groups at the end. This study highlights the desirability of further research on this issue and the importance of diagnosing and treating iron deficiency as quickly as possible, as its effects in the nervous system may remain in spite of iron level equalization [47].

Studies on the effects of iron deficiency on sleep are also present in the literature. J. I. Rodrigues Jr. and others indicate that insufficient iron levels result in shortened and reduced sleep quality in children during the first year of life [48].

Studies assessing the effects of iron deficiency on the cardiovascular system and heart function are also present in the literature. This study evaluated 135 children of similar age who were presented to the Paediatric Cardiology Department. Participants were divided into three groups according to their ferritin levels. Surface electrocardiography (ECG) and transthoracic echocardiogram were used for assessment to compare cardiac repolarization parameters. Some

of the parameters differed in the group with low ferritin levels, suggesting that iron deficiency may be associated with a tendency towards arrhythmias in children without structural heart defects. [49]

In 2020 and 2021, researchers analyzed 12 studies (using data from 9981 children) to determine the impact of iron deficiency on early childhood caries (ECC). As conclusions, they found that children with ECC had lower iron levels than the control group. Iron deficiency was more common in children with ECC. However, the relationship is poorly understood. Iron deficiency may coexist with early childhood caries due to similar causes: malnutrition and low socioeconomic status. However, the role of iron in normal salivary gland function and the anti-carious properties of this micronutrient are emphasized. This issue requires more observations and analysis [50].

**Methods of preventions**

Iron deficiency is a global problem with major public health importance. [23] It is most prevalent in low-developed countries. [41] The first step in ID prevention strategies is a varied and nutritious diet, based on iron-containing products with high bioavailability. [23] The diet and availability of different valuable foods is frequently limited by economic, cultural and social factors. For this reason, methods of fortifying food with essential macronutrients are becoming increasingly common. Research shows that eating iron-fortified foods is one of the most effective methods of ID prevention. Examples of such foods include cereals, dairy products, flour, bread and spices. They contain elemental iron or ingredients that facilitate the absorption of iron from food. Iron-rich infant formula products are used in infants. [51]

M.M.A. Machado et al. assessed 162 Brazilian children to evaluate the effectiveness of Multiple Micronutrient Powder (MMP) in the prevention and treatment of iron deficiency. The sachet contained iron as well as other compounds such as folic acid, ascorbic acid, retinol, copper, sodium, potassium, zinc and others. The children consumed it mixed with rice or vegetable purée. For comparison, the standard of supplementation was ferrous sulfate associated with folic acid. (FS_FA). The study, which lasted an average of 15 weeks, showed that the use of MMP is as effective as FS_FA in increasing haemoglobin and ferritin levels in children. The use of powders is one of the strategies for preventing iron deficiency in various countries around the world. Research confirms that they have a positive effect on ID and

anaemia in any case. The sachets are easy to use, have a clear dosage and compensate for the status of many micronutrients needed, not just iron. [52]

Prevention also includes care for a group of children at high risk of ID. This includes, for example, premature and low birth weight babies. Studies show that iron supplementation reduces the risk of deficiency. The recommended dose is 2 mg/kg per day from 6 weeks to 6 months. Dosage and duration of supplementation is determined individually. Treatment should be closely monitored due to the weak antioxidant mechanisms in preterm infants and the risk of overdose. [53] Maternal iron imbalance during pregnancy is a further risk factor for deficiency in children. The third trimester is a period of intensive transfer of maternal iron to the fetus. Supplementation during pregnancy restores the iron balance to normal levels. The WHO recommended daily dose of supplementation is 30-60 mg of elemental iron and 400 µg of folic acid. [54]

The topic of the effect of delayed umbilical cord clamping on iron status in newborns is eagerly studied and discussed. The papers agree that delaying the clamping of the umbilical cord by about 1-3 minutes after birth improves the iron reserves of the newborn. [53] Delayed clamping of the umbilical cord improved hemoglobin, ferritin and MCV levels in infants at birth. [54] This intervention prevents the onset of iron deficiency in infants up to 6 months of age but has no effect on subsequent child development. This benefit is particularly important in children from ID risk groups, e.g.: preterm infants, low birth weight babies.[55]

**Treatment**

Treatment of iron deficiency involves identifying and eliminating the cause and balancing the body's iron levels. [56] Iron supplementation can be provided by several routes: orally, parenterally and by red cell concentrate transfusion. [13]

Oral iron is the first line treatment in a major of deficiency cases. This method is widely available, inexpensive, easy to administer and safe. [57] The appropriate dose of iron should be calculated in reference to elemental iron. The daily therapeutic dose of elemental iron is 3-6 mg/kg body weight (BW) given in 1-3 divided doses. The maximum daily dose of elemental iron equals 150-200 mg. In iron salt preparations, the recommended dose is different: for $Fe^{2+}$ salts 2-3 mg/kg BW and $Fe^{3+}$ salts 3-5 mg/kg BW. The personalized dosage is determined by the doctor after individual assessment of the patient.[25] To maximize absorption, iron should

be taken on an empty stomach or between meals. However, eating it after food may reduce the risk of side effects. [58]

Iron salts are the most frequently used. However, to enhance the stability and absorption of the preparations, also chelated forms of iron are used, i.e. combining it with amino acids. [51] Examples of available preparations include ferrous ascorbate, ferrous fumarate, ferrous gluconate, ferrous sulfate, Polysaccharide-iron complex, carbonyl iron, iron proteinsuccinylate, iron amino acid chelates (ferrousbisglycinate, ferrictrisglycinate). [57].

Gastrointestinal side effects with this supplementation are common: constipation, nausea, abdominal pain, diarrhoea. New dosage methods are being tested all the time. Studies are reported in which iron intake every other day had similar absorption efficiencies to daily intake, but the primary method had significantly fewer side effects. This is related to the regulating effect of hepcidin, which can reduce absorption at high doses of supplementation through the saturability of intestinal absorption [59]

Evaluation of the effects of oral therapy is performed after a minimum of one month of treatment. [61] A complete blood count (CBC) after 1 month should demonstrate an increase in haemoglobin of 1 g/dl. [60] The intravenous route of iron administration is recommended when there is no response to oral therapy. This may be due to poor adherence to systematic and regular intake or the occurrence of severe side effects. Parenteral administration is the first choice in children with severe anaemia or the occurrence of general conditions with a severe course, e.g. gastrointestinal malabsorption, concomitant inflammatory diseases or chronic kidney disease. [61]

Infusion preparation examples in children: iron dextran, iron sucrose, ferric gluconate, ferric carboxymaltose. Ferric carboxymaltose is becoming increasingly popular because of the safe administration of a high dose of iron in a single, rapid infusion. [21]

The advantages of intravenous therapy are rapid replenishment of iron stores and fewer gastrointestinal side effects. [60] Disadvantages include the higher treatment cost, the risk of infusion-related hypersensitivity reactions and an increased chance of iron overload or poisoning. The procedure is performed by qualified healthcare professionals. [21]

A study was conducted in Texas to evaluate the safety and efficacy of intravenous ferric carboxymaltose (FCM) in children. 72 patients in whom oral iron therapy was ineffective received FCM infusions. In 98% of the patients, there was an improvement in blood parameters. Only 16% of participants experienced mild and quickly resolving side effects. The authors of the study emphasise that oral iron preparations are the first-line treatment and intravenous therapy is used for patients in whom this treatment has failed. [62]

Dietary advice and the enforcement of appropriate habits are important with any method of iron supplementation. However, these are not sufficient to raise serum ferritin levels. Two groups of children were compared - the first who received dietary advice and liquid ferrous sulphate orally and the second who received advice and a liquid placebo. At the end of the study, the first group had an average ferritin level 16.9 μg/l higher than the control one. [63]

## Conclusion

Iron deficiency is a prevalent problem among children that can lead to serious health consequences. A frequent consequence is anaemia. Children aged 6 months to 5 years are most at risk due to their intensive growth and development. ID is particularly widespread in low- and middle-income countries where socioeconomic and cultural problems affect the quality of the diet. Currently, great emphasis is placed on the prevention of deficiencies and their early detection. Children at risk of ID are provided with special care. Appropriately selected nutrition plans are being introduced, and iron-enriched foods are being tested. With the current indications, children receive individually tailored supplementation. Iron is crucial for the functioning of many body systems; therefore, its deficiency causes various symptoms. The most serious effects are related to disorders of brain development, memory and cognitive functions. Effective elimination of iron deficiency is extremely important because there are studies that suggest that the effects of deficiency in childhood may last a lifetime.

## DISCLOSURES:

### Authors contributions

Conceptualization, Anna Dziewierz and Paulina Dziewierz; methodology, Patrycja Pietrusińska; software, Adam Sobiński; check, Aleksandra Welkier, Patrycja Śliwa-Tytko and Jakub Moder; formal analysis, Aleksandra Dudek; investigation, Jakub Moder; resources, Anna Dziewierz; data curation, Aleksandra Sadowska; writing - rough preparation, Anna Dziewierz and Paulina Dziewierz; writing - review and editing, Patrycja Pietrusińska; visualization, Joanna Miśkiewiecz; supervision, Paula Kwaśniewska and Adam Sobiński; project administration, Patrycja Śliwa -Tytko.

All authors have read and agreed with the published version of the manuscript.

**Funding Statement:** The study did not receive special funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** The data presented in this study is available upon request from the corresponding author.

**Acknowledgments:** Not applicable.

**Conflict of Interest Statement:** All authors declare that they have no conflicts of interest

---

**References**

1. Cerami C. Iron Nutriture of the Fetus, Neonate, Infant, and Child. Ann Nutr Metab. 2017;71 Suppl 3(Suppl 3):8-14. doi: 10.1159/000481447. Epub 2017 Dec 22.
2. Lane DJ, Merlot AM, Huang ML, Bae DH, Jansson PJ, Sahni S, Kalinowski DS, Richardson DR. Cellular iron uptake, trafficking and metabolism: Key molecules and mechanisms and their roles in disease. Biochim Biophys Acta. 2015 May;1853(5):1130-44. doi: 10.1016/j.bbamcr.2015.01.021.
3. Vogt AS, Arsiwala T, Mohsen M, Vogel M, Manolova V, Bachmann MF. On Iron Metabolism and Its Regulation. Int J Mol Sci. 2021 Apr 27;22(9):4591. doi: 10.3390/ijms22094591.
4. Venkataramani V. Iron Homeostasis and Metabolism: Two Sides of a Coin. Adv Exp Med Biol. 2021;1301:25-40. doi: 10.1007/978-3-030-62026-4_3.
5. Esa Soppi. Iron Deficiency Without Anemia – Common, Important, Neglected. Clin Case Rep Rev 5: DOI: 10.15761/CCRR.1000456
6. Gao G, Li J, Zhang Y, Chang YZ. Cellular Iron Metabolism and Regulation. Adv Exp Med Biol. 2019;1173:21-32. doi: 10.1007/978-981-13-9589-5_2.
7. Garofalo V, Condorelli RA, Cannarella R, Aversa A, Calogero AE, La Vignera S. Relationship between Iron Deficiency and Thyroid Function: A Systematic Review and Meta-Analysis. Nutrients. 2023 Nov 15;15(22):4790. doi: 10.3390/nu15224790.
8. Percy L, Mansour D, Fraser I. Iron deficiency and iron deficiency anaemia in women. Best Pract Res Clin Obstet Gynaecol. 2017 Apr;40:55-67. doi: 10.1016/j.bpobgyn.2016.09.007.
9. Means RT, Iron Deficiency and Iron Deficiency Anemia: Implications and Impact in Pregnancy, Fetal Development, and Early Childhood Parameters. Nutrients. 2020 Feb 11;12(2):447. doi: 10.3390/nu12020447.
10. Camaschella C. Iron-deficiency anemia. N Engl J Med. 2015 May 7;372(19):1832-43. doi: 10.1056/NEJMra1401038.

11. Briguglio M, Hrelia S, Malaguti M, Lombardi G, Riso P, Porrini M, Perazzo P, Banfi G. The Central Role of Iron in Human Nutrition: From Folk to Contemporary Medicine. Nutrients. 2020 Jun 12;12(6):1761. doi: 10.3390/nu12061761.
12. Rajagukguk YV, Arnold M, Gramza-Michałowska A. Pulse Probiotic Superfood as Iron Status Improvement Agent in Active Women-A Review. Molecules. 2021 Apr 7;26(8):2121. doi: 10.3390/molecules26082121.
13. Kumar A, Sharma E, Marley A, Samaan MA, Brookes MJ. Iron deficiency anaemia: pathophysiology, assessment, practical management. BMJ Open Gastroenterol 2022 Jan; 9(1). doi.org/10.1136/bmjgast-2021-000759.
14. Piskin E, Cianciosi D, Gulec S, Tomas M, Capanoglu E. Iron Absorption: Factors, Limitations, and Improvement Methods. ACS Omega. 2022 Jun 10;7(24):20441-20456. doi: 10.1021/acsomega.2c01833
15. Fairweather-Tait, S., & Sharp, P. (2021). Iron. In N. A. M. Eskin (Ed.), The Latest Research and Development of Minerals in Human Nutrition (Vol. 96, pp. 219-250). Chapter in book
16. Atkins LA, Spence AC, Szymlek-Gay EA. Iron Nutrition of Pre-Schoolers in High-Income Countries: A Review. Nutrients. 2023 Jun 2;15(11):2616. doi: 10.3390/nu15112616.
17. Ahmad Fuzi SF, Koller D, Bruggraber S, Pereira DI, Dainty JR, Mushtaq S. A 1-h time interval between a meal containing iron and consumption of tea attenuates the inhibitory effects on iron absorption: a controlled trial in a cohort of healthy UK women using a stable iron isotope. Am J Clin Nutr. 2017 Dec;106(6):1413-1421. doi: 10.3945/ajcn.117.161364.
18. Nutrient Lists from Standard Reference Legacy (2018) from National Agricultural Library - Iron https://www.nal.usda.gov/human-nutrition-and-food-safety/nutrient-lists-standard-reference-legacy-2018 (Access: 01.02.2025r)
19. Leung AKC, Lam JM, Wong AHC, Hon KL, Li X. Iron Deficiency Anemia: An Updated Review. Curr Pediatr Rev. 2024;20(3):339-356. doi: 10.2174/1573396320666230727102042.
20. Jullien S. Screening of iron deficiency anaemia in early childhood. BMC Pediatr. 2021 Sep 8;21(Suppl 1):337. doi: 10.1186/s12887-021-02725-w.
21. Taylor S, Rampton D. Treatment of iron deficiency anemia: practical considerations. Pol Arch Med Wewn. 2015;125(6):452-60. doi: 10.20452/pamw.2888.

22. Singer CE, Biciuşcă V, Abdul-Razzak J, Popescu IAS, Georgmăneanu C, Singer MM, Mărginean CM, Popescu M. Associated factors in pediatric patients admitted with severe iron-deficiency anemia in the last seven years - the experience of a single pediatric unit. Rom J Morphol Embryol. 2023 Jul-Sep;64(3):419-426. doi: 10.47162/RJME.64.3.13.
23. Chouraqui JP. Dietary Approaches to Iron Deficiency Prevention in Childhood-A Critical Public Health Issue. Nutrients. 2022 Apr 12;14(8):1604. doi: 10.3390/nu14081604.
24. Bastian TW, Rao R, Tran PV, Georgieff MK. The Effects of Early-Life Iron Deficiency on Brain Energy Metabolism. Neurosci Insights. 2020 Jun 29;15:2633105520935104. doi: 10.1177/2633105520935104.
25. Chaber R, Helwich E, Lauterbach R, Mastalerz-Migas A, Matysiak M, Peregud-Pogorzelski J, Styczyński J, Szczepański T, Jackowska T. Diagnosis and Treatment of Iron Deficiency and Iron Deficiency Anemia in Children and Adolescents: Recommendations of the Polish Pediatric Society, the Polish Society of Pediatric Oncology and Hematology, the Polish Society of Neonatology, and the Polish Society of Family Medicine. Nutrients. 2024 Oct 25;16(21):3623. doi: 10.3390/nu16213623.
26. Mattiello V, Schmugge M, Hengartner H, von der Weid N, Renella R; SPOG Pediatric Hematology Working Group. Diagnosis and management of iron deficiency in children with or without anemia: consensus recommendations of the SPOG Pediatric Hematology Working Group. Eur J Pediatr. 2020 Apr;179(4):527-545. doi: 10.1007/s00431-020-03597-5.
27. Subramaniam G, Girish M. Iron deficiency anemia in children. Indian J Pediatr. 2015 Jun;82(6):558-64. doi: 10.1007/s12098-014-1643-9.
28. WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations https://www.who.int/publications/i/item/9789240000124 (Access: 28.01.2025r)
29. Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology Am Soc Hematol Educ Program. 2015;2015:8-13. doi: 10.1182/asheducation-2015.1.8.
30. Cappellini MD, Musallam KM, Taher AT. Iron deficiency anaemia revisited. J Intern Med. 2020 Feb;287(2):153-170. doi: 10.1111/joim.13004.
31. Fletcher A, Forbes A, Svenson N, Wayne Thomas D; A British Society for Haematology Good Practice Paper. Guideline for the laboratory diagnosis of iron deficiency in adults

(excluding pregnancy) and children. Br J Haematol. 2022 Feb;196(3):523-529. doi: 10.1111/bjh.17900.

32. Iriarte-Gahete M, Tarancon-Diez L, Garrido-Rodríguez V, Leal M, Pacheco YM. Absolute and functional iron deficiency: Biomarkers, impact on immune system, and therapy. Blood Rev. 2024 Nov;68:101227. doi: 10.1016/j.blre.2024.101227.
33. Subramaniam G, Girish M. Iron deficiency anemia in children. Indian J Pediatr. 2015 Jun;82(6):558-64. doi: 10.1007/s12098-014-1643-9.
34. Gattermann N, Muckenthaler MU, Kulozik AE, Metzgeroth G, Hastka J. The Evaluation of Iron Deficiency and Iron Overload. Dtsch Arztebl Int. 2021 Dec 10;118(49):847-856. doi: 10.3238/arztebl.m2021.0290.
35. Gallagher PG. Anemia in the pediatric patient. Blood. 2022 Aug 11;140(6):571-593. doi: 10.1182/blood.2020006479.
36. Al-Naseem A, Sallam A, Choudhury S, Thachil J. Iron deficiency without anaemia: a diagnosis that matters. Clin Med (Lond). 2021 Mar;21(2):107-113. doi: 10.7861/clinmed.2020-0582.
37. Premjeyanth V, Shipman A. Iron deficiency without anaemia. Clin Med (Lond). 2021 Jul;21(4):e427. doi: 10.7861/clinmed.Let.21.4.3.
38. Borgna-Pignatti C, Zanella S. Pica as a manifestation of iron deficiency. Expert Rev Hematol. 2016 Nov;9(11):1075-1080. doi: 10.1080/17474086.2016.1245136.
39. The Association Between Pica and Iron-Deficiency Anemia: A Scoping Review - Pallavi R Ganesan 1,✉, Audrey A Vasauskas 1
40. Moreno-Fernandez J, Ochoa JJ, Latunde-Dada GO, Diaz-Castro J. Iron Deficiency and Iron Homeostasis in Low Birth Weight Preterm Infants: A Systematic Review. Nutrients. 2019 May 16;11(5):1090. doi: 10.3390/nu11051090.
41. Sundararajan S, Rabe H. Prevention of iron deficiency anemia in infants and toddlers. Pediatr Res. 2021 Jan;89(1):63-73. doi: 10.1038/s41390-020-0907-5.
42. McWilliams S, Singh I, Leung W, Stockler S, Ipsiroglu OS. Iron deficiency and common neurodevelopmental disorders-A scoping review. PLoS One. 2022 Sep 29;17(9):e0273819. doi: 10.1371/journal.pone.0273819.
43. McCann S, Perapoch Amadó M, Moore SE. The Role of Iron in Brain Development: A Systematic Review. Nutrients. 2020 Jul 5;12(7):2001. doi: 10.3390/nu12072001.
44. Shah HE, Bhawnani N, Ethirajulu A, Alkasabera A, Onyali CB, Anim-Koranteng C, Mostafa JA. Iron Deficiency-Induced Changes in the Hippocampus, Corpus Striatum,

and Monoamines Levels That Lead to Anxiety, Depression, Sleep Disorders, and Psychotic Disorders. Cureus. 2021 Sep 20;13(9):e18138. doi: 10.7759/cureus.18138.

45. Pivina L, Semenova Y, Doşa MD, Dauletyarova M, Bjørklund G. Iron Deficiency, Cognitive Functions, and Neurobehavioral Disorders in Children. J Mol Neurosci. 2019 May;68(1):1-10. doi: 10.1007/s12031-019-01276-1.
46. I East P, Lozoff B, Blanco E, Delker E, Delva J, Encina P, Gahagan S. Infant iron deficiency, child affect, and maternal unresponsiveness: Testing the long-term effects of functional isolation. Dev Psychol. 2017 Dec;53(12):2233-2244. doi: 10.1037/dev0000385.
47. Gingoyon A, Borkhoff CM, Koroshegyi C, Mamak E, Birken CS, Maguire JL, Fehlings D, Macarthur C, Parkin PC. Chronic Iron Deficiency and Cognitive Function in Early Childhood. Pediatrics. 2022 Dec 1;150(6):e2021055926. doi: 10.1542/peds.2021-055926.
48. Rodrigues Junior JI, Mecenas VGF, de Oliveira Lima M, Menezes RCE, Oliveira PMB, Longo-Silva G. Association between iron deficiency anemia and sleep duration in the first year of life. Rev Paul Pediatr. 2023 Jul 24;42:e2022173. doi: 10.1590/1984-0462/2024/42/2022173.
49. Demir F, Kayali S, Gokcebay DG. Does Iron Deficiency Affect the Heart in Children? J Pediatr Hematol Oncol. 2022 Apr 1;44(3):84-88. doi: 10.1097/MPH.0000000000002170.
50. Ji SQ, Han R, Huang PP, Wang SY, Lin H, Ma L. Iron deficiency and early childhood caries: a systematic review and meta-analysis. Chin Med J 2021; 134:2832–2837. doi: 10.1097/CM9.0000000000001729
51. Man Y, Xu T, Adhikari B, Zhou C, Wang Y, Wang B. Iron supplementation and iron-fortified foods: a review. Crit Rev Food Sci Nutr. 2022;62(16):4504-4525. doi: 10.1080/10408398.2021.1876623.
52. Machado MMA, Lopes MP, Schincaglia RM, da Costa PSS, Coelho ASG, Hadler MCCM. Effect of Fortification with Multiple Micronutrient Powder on the Prevention and Treatment of Iron Deficiency and Anaemia in Brazilian Children: A Randomized Clinical Trial. Nutrients. 2021 Jun 23;13(7):2160. doi: 10.3390/nu13072160.
53. Andersson O, Lindquist B, Lindgren M, Stjernqvist K, Domellöf M, Hellström-Westas L. Effect of Delayed Cord Clamping on Neurodevelopment at 4 Years of Age: A Randomized Clinical Trial. JAMA Pediatr. 2015 Jul;169(7):631-8. doi: 10.1001/jamapediatrics.2015.0358.

54. Fu X, Dang D, Li S, Xu Z, Wu H. Effect of Delayed Versus Early Cord Clamping on Improving Anemia in Term Infants Aged Two Months or Older - A Meta-analysis. Indian Pediatr. 2020 Sep 15;57(9):815-819.
55. Kc A, Rana N, Målqvist M, Jarawka Ranneberg L, Subedi K, Andersson O. Effects of Delayed Umbilical Cord Clamping vs Early Clamping on Anemia in Infants at 8 and 12 Months: A Randomized Clinical Trial. JAMA Pediatr. 2017 Mar 1;171(3):264-270. doi: 10.1001/jamapediatrics.2016.3971.
56. Low MS, Grigoriadis G. Iron deficiency and new insights into therapy. Med J Aust. 2017 Jul 17;207(2):81-87. doi: 10.5694/mja16.01304.
57. Iolascon A, Andolfo I, Russo R, Sanchez M, Busti F, Swinkels D, Aguilar Martinez P, Bou-Fakhredin R, Muckenthaler MU, Unal S, Porto G, Ganz T, Kattamis A, De Franceschi L, Cappellini MD, Munro MG, Taher A; from EHA-SWG Red Cell and Iron. Recommendations for diagnosis, treatment, and prevention of iron deficiency and iron deficiency anemia. Hemasphere. 2024 Jul 15;8(7):e108. doi: 10.1002/hem3.108.
58. Warner MJ, Kamran MT. Iron Deficiency Anemia. 2023 Aug 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
59. Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. Lancet. 2021 Jan 16;397(10270):233-248. doi: 10.1016/S0140-6736(20)32594-0.
60. Subramaniam G, Girish M. Iron deficiency anemia in children. Indian J Pediatr. 2015 Jun;82(6):558-64. doi: 10.1007/s12098-014-1643-9.
61. Clay T Cohen, Jacquelyn M Powers. Intravenous iron therapy in pediatrics: who should get it and when is the right time. Hematology 2023(1):630-635. DOI:10.1182/hematology.2023000496
62. Powers JM, Shamoun M, McCavit TL, Adix L, Buchanan GR. Intravenous Ferric Carboxymaltose in Children with Iron Deficiency Anemia Who Respond Poorly to Oral Iron. J Pediatr. 2017 Jan;180:212-216. doi: 10.1016/j.jpeds.2016.09.053.
63. Parkin PC, Borkhoff CM, Macarthur C, Abdullah K, Birken CS, Fehlings D, Koroshegyi C, Maguire JL, Mamak E, Mamdani M, Thorpe KE, Zlotkin SH, Zuo F; TARGet Kids! Collaboration. Randomized Trial of Oral Iron and Diet Advice versus Diet Advice Alone in Young Children with Nonanemic Iron Deficiency. J Pediatr. 2021 Jun;233:233-240.e1. doi: 10.1016/j.jpeds.2021.01.073.