

IRON DEFICIENCY ANEMIAS IN CHILDREN WITH GASTROINTESTINAL DISEASES

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Abstract

Iron deficiency anemia is a pathological condition in which the level of iron in the body, the concentration of red blood cells and hemoglobin in the blood decreases. IDA is the most common type of anemia and the most common disease in the world associated with a lack of nutrients. Iron is an indispensable element that can be obtained only with food. Often, in diseases of the gastrointestinal tract, the process of absorption of this element is disrupted, which leads to anemia. In this article we consider the pathogenesis of the development of iron deficiency anemia in pathologies of the digestive system.

Keywords: Iron deficiency anemia, gastrointestinal tract diseases, gastritis, *Helicobacter pylori*, malabsorption

Relevance: One third of the world's population suffers from anemia; 800 million of the total numbers of patients are women and children. According to WHO data, 21.9% of children aged 6 to 59 months had IDA in 2019. IDA also accounted for 42% of all anemias in under 5 years children. In such conditions, IDA becomes not only a medical problem, but also a global problem. Patients with IDA need adequate diagnosis and professional treatment.

Aim of the study: To determine the relationship between the occurrence of IDA in children and gastrointestinal diseases. To identify diseases of the digestive system that most often lead to anemia.

Materials and methods: Results of general blood analysis, serum iron level, serum ferritin level, transferrin saturation, number of reticulocytes, width of erythrocyte distribution by volume (RDW) and peripheral blood smear in 75 patients aged 15 to 17 years who applied to the 1st clinic of SamSMU in the period from April to July 2023 with complaints of various disorders in the functioning of the gastrointestinal tract.

Analysis of data provided on the official pages of WHO and UNICEF. The article also includes available metadata.

Results and discussions: For a long time there have been diseases caused by a lack of various substances, such as micro and macro elements, vitamins, macronutrients of food, etc. However, the most striking example, of course, is iron deficiency - the most common pathology in the world with a lack of nutrients. In children with a lack of iron, an iron deficiency condition is soon formed, which turns into iron deficiency anemia. Iron deficiency anemia (IDA) is a disease characterized by reduced iron content in blood serum, tissue depots and bone marrow. The main symptoms of IDA are pallor of the skin, shortness of breath, fatigue, weakness. In addition, there may be restless legs syndrome (an unpleasant urge to move the legs during periods of inactivity), pica - a perversion of taste, cheilitis, glossitis, koilonychia – concave nails.

Infants, children aged less than 2 years, less than 5 years and adolescents are most prone to anemia. In children under 2 years of age, IDA occurs due to an increased need for iron due to rapid growth and development. Moreover, children of this age group are often improperly fed. Their complementary foods contain little iron and many inhibitors of its absorption. Teenagers

also need iron because of accelerated growth. According to many studies, there is a strong link between IDA and reduced cognitive and motor development in children. In such patients, alterations of brain structures are observed, which is irreversible even when treated with iron preparations.

In a healthy person, iron is constantly exchanged in a closed system. They lose about 1-1.5 mg of the element per day, in the absence of blood loss and other pathologies. The consumed iron is replenished at the expense of iron coming from the outside. Its sources are divided into 2 groups: exogenous and endogenous. Endogenous sources include hemoglobin and iron-containing depots, whereas exogenous sources include alimentary (food) iron. Due to the presence of an intestinal barrier, only 10% of iron is absorbed from the average amount of 10-15 mg contained in the daily human diet. Moreover, iron is mainly (90%) absorbed in the duodenum and in a smaller amount (10%) in the proximal parts of the jejunum. First of all, it gets from the intestinal cavity into the enterocyte, and then it is sent to the blood plasma. Hem iron is best absorbed, followed by Fe(II) and Fe(III).

An interesting fact is that the necessary level of iron in the body is regulated not by its excretion, but by absorption. The absorption of iron depends not only on its amount in food, but also on its bioavailability. This process is controlled by special receptors located on the surface of the mucous membrane of the digestive tract. These receptors are responsible for the accumulation of iron in the body. In physiological (rapid growth, pregnancy, menstruation) or pathological (blood loss) conditions, when the need for iron increases and its reserves in the body are depleted, iron absorption increases by 10-20%. And in the opposite case, when the amount of iron in the body increases, its absorption decreases sharply. It follows from this that the absorption of iron is inversely proportional to its amount in the body. However, in the case when a patient consumes a sufficient amount of iron, but he has IDA, the main causes may be agastric conditions, atrophic changes in the mucous membrane of the digestive tract, achilia, enteritis, anenteral conditions, etc.

Table 1. Hemoglobin level in the diagnosis of anemia according to WHO

Age	No anemia	Mild	Moderate	Severe
6-59 months	≥ 110	100-109	70-99	< 70
5-11 years	≥ 115	110-114	80-109	< 80
12-14 years	≥ 120	110-119	80-109	< 80
After 15 years	≥ 120	110-119	80-109	< 80

The table above contains data provided by WHO to determine the degree of anemia in children. Thus, in our studies, anemia in the analyzed group was mild in 70% of cases, moderate in 26% and severe in 4%.

The following diseases of the digestive tract are often accompanied by IDA: gastric ulcer or duodenal ulcer, polyps, tumors and diverticula of the stomach and intestines, malabsorption (celiac disease), erosive esophagitis and gastritis, Mallory-Weiss syndrome, postresection condition, inflammatory bowel diseases. Studies conducted in Israel show that in 4-6% of patients with idiopathic IDA, celiac disease is diagnosed. 10% of patients with IDA in Iran also had celiac disease. Dysbiosis also contributes to the development of IDA, which further impairs digestion and absorption into the bloodstream. On the other hand, not only gastrointestinal diseases lead to a lack of iron, but iron deficiency in turn causes dysbiosis, which then leads to

dyspeptic phenomena and inflammation of the intestinal walls. The so-called "vicious circle" is formed, in which pathological phenomena in the digestive system worsen the absorption of iron, its deficiency occurs, which leads to dysbiosis and contributes to further insufficient absorption of iron. Blood loss is also a common cause of iron deficiency in the body. Chronic latent bleeding is characteristic of such diseases of the gastrointestinal tract as gastric ulcer or duodenal ulcer, malignant neoplasms, etc. Less often, iron absorption decreases with improper and insufficient nutrition.

According to our data, IDA was detected in 46 patients, which was 61% of the total number. Of these, 9 patients (20%) had gastric or duodenal ulcer, 14 patients (30%) had gastritis, and 5 patients had inflammatory bowel diseases (11%). *Helicobacter pylori* infection was detected in 8 out of 14 patients with gastritis. Based on anamnesis, it turned out that 10 patients (22%) regularly took NSAIDs and 5 patients (11%) were treated with antibiotics. These two groups of drugs also have a negative effect on the mucous membrane. The patients' eating habits were also studied: 22 patients reported frequent consumption of unhealthy food, another 6 reported eating disorders. Malabsorption syndrome was observed in 30 patients.

Table 2. Unicef data on anemia among children from 6 to 59 months. Uzbekistan. 2017

Anemia	14,7%	♂	16,1%
		♀	13,1%
Ferrum deficiency	54,7%	♂	57%
		♀	51,7%
Ferrum deficiency anemia	10,8%	♂	12,1%
		♀	9,3%

According to data for 2017 in the Republic of Uzbekistan, more than half of children aged 6-59 months had iron deficiency in the body. To date, this figure has been increased.

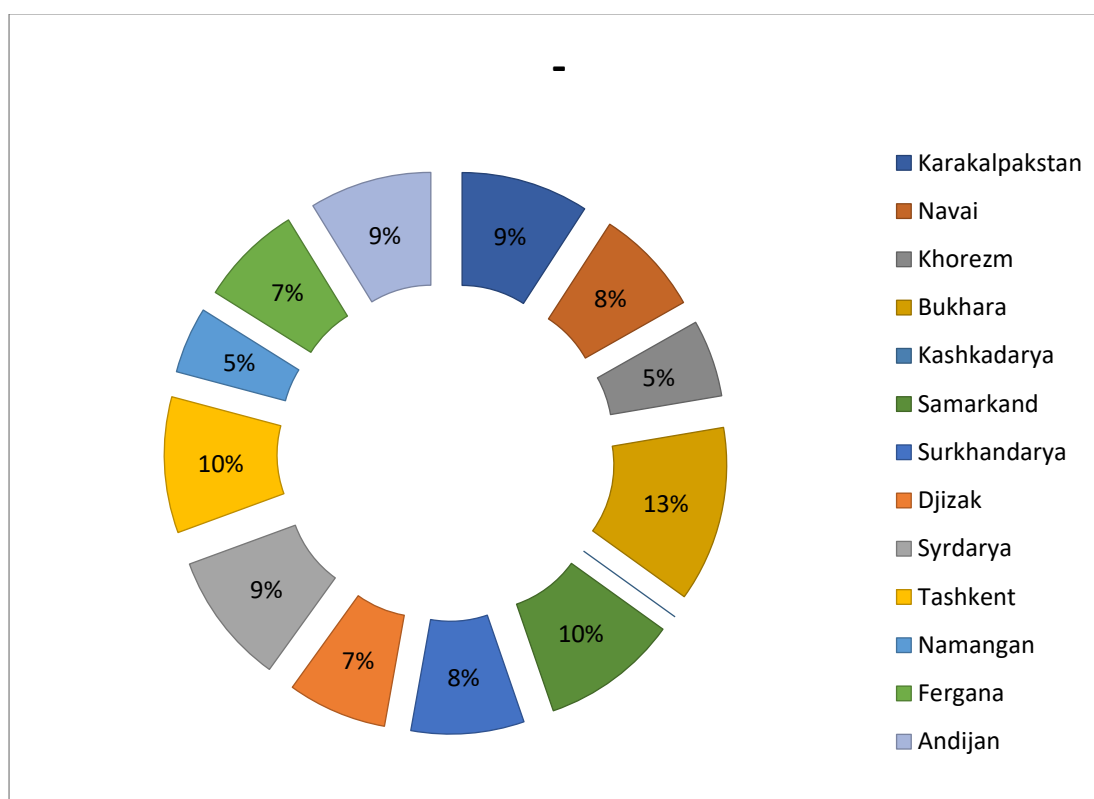
The causes of IDA, as well as B12-deficient anemia in the stomach are atrophic changes. Hydrochloric acid of the stomach converts trivalent iron into a divalent form for better absorption. Moreover, hydrochloric acid and gastric juice proteases promote the release of vitamin B12 from food and transfer it to the internal factor for subsequent transportation. So, in the fundal part of the stomach there are parietal cells that secrete an internal factor (gastric juice glycoprotein). If these cells are damaged, then an insufficient amount of acid and internal factor is secreted. In addition to hydrochloric acid, ascorbic acid is necessary for the absorption of iron. Against the background of chronic inflammation of the gastric mucosa, the concentration of ascorbic acid also decreases. Such injuries are characteristic of atrophic gastritis. Atrophic gastritis, in turn, is the result of two processes: prolonged persistence of *Helicobacter pylori* or autoimmune disorders. With autoimmune gastritis, antibodies to parietal cells, internal factor, H⁺/K⁺-ATPase are formed, as a result of which parietal cells are reduced, hypo- or achlorhydria are formed, the level of cobalamin decreases.

With prolonged infection with *H. Pylori*, an inflammatory process is formed, and parietal cells are also reduced. 75-100% of cases of chronic gastritis are associated with this infection. More

than half of the world's population is infected with *H. pylori*. In children, this figure reaches 60-70%. At the age of 7-11 years, children with gastrointestinal diseases are infected in more than 50%, and children of high school age in 80%. C. Hershko and A. Ronson found the presence of active *Helicobacter pylori* infection in 50% of patients with anemia of unclear etiology; autoimmune gastritis was detected in 20-27%. W. Xia et al. *H. Pylori* infection was found in 46.9% of adolescent girls with IDA. Then they performed eradication therapy, which led to better absorption of iron preparations. In the studies of G. Vitale et al. eradication therapy increased the level of iron in the blood serum. In addition, *H. Pylori* competes with the host for the use of iron. Iron is used by the microorganism for its own growth and development. Thus, when labeled iron was introduced into the body, its transition from bone marrow to bacteria was detected. The reason is that *H. Pylori* is a more active genetic system that consumes iron, because of this it adapts better in the human stomach. The bacterium also has a mutant protein Fur (ferric uptake regulator), which regulates iron intake. In this case, even with an overabundance of this element, the bacterium does not stop taking it. Thanks to all the studies conducted in this direction in 2010, international experts on the study of *Helicobacter pylori* included IDA in the list of additional indications for eradication therapy.

The development of anemia is accompanied by inflammatory bowel diseases (IBD), such as ulcerative colitis (ulcerative colitis) and Crohn's disease (CD). S.Schreiber et al. anemia was found in 25% of patients with CD and 37% of patients with NAC. There are several mechanisms that cause anemia in IBD. The first mechanism is a violation of the absorption of essential nutrients, especially iron, vitamin B12 and folic acid. In some cases, the absorption of proteins, fats and carbohydrates is disrupted. With a lack of proteins, a protein-energy deficiency is formed, leading to hypotransferrinemia, further to a violation of iron transport and a violation of erythropoiesis. The second mechanism is prolonged blood loss, especially common in IBD. The third mechanism is the so-called AHZ (anemia of chronic diseases). Such anemia is formed due to a prolonged increase in the level of proinflammatory cytokines and proteins of the acute phase of inflammation (hepsidin). They lead to inadequate iron metabolism and inhibition of erythropoiesis. Hepsidin prevents the absorption of iron in the duodenum, blocks the release of iron from macrophages and inhibits its absorption by the bone marrow. With AHZ, the level of serum iron and transferrin saturation with iron decreases. However, ferritin levels vary within normal limits. In pediatrics, about 20% of all anemia is AHZ. According to the Russian Children's Clinical Hospital (RDCB) for two decades, 35% of children with NAC had IDA.

Figure 1. UNICEF data on the spread of anemia among children from 6 to 59 months in Uzbekistan for 2017



After proper diagnosis, patients in the treatment of iron deficiency conditions are recommended to consume products with its high content (meat, tongue, liver) and iron-containing preparations. It is also necessary to find out the cause of anemia. Often the root of the problem is a violation of digestive processes. To enhance the effect of treatment, it is necessary to use funds for the treatment of dysbiosis.

Conclusions: The number of children suffering from iron deficiency conditions increases every year. Often the cause of anemia is unknown and they are not eliminated by standard therapy with the use of iron-containing drugs. In such cases, the attending physician should think about possible disorders in the digestive system, which often lead to IDA. We recommend examination of the digestive system in patients with prolonged anemia of unclear etiology, as well as determination of the titer of *Helicobacter pylori* for a more accurate assessment of the patient's condition.

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