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«PECULIARITIES OF CHILDHOOD ANEMIA IN CONDITIONS OF MARTIAL LAW»

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CONTENT

LIST OF SYMBOLS

CBC	Complete blood count
CRCH	Chernivtsi Regional Children's Hospital
CRP	C-reactive protein
DS	Deficiency state
ECG	Electrocardiographic
ESR	Erythrocyte sedimentation rate
EU	European Union
G6PD	Glucose-6-phosphate dehydrogenase
Hb	Hemoglobin
Hct	Hematocrit
HSCT	Hematopoietic stem cell transplantation
IDA	Iron def anemia
IDP	internally displaced person
IVIG	Intravenous immunoglobulin
LDH	Lactate dehydrogenase
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MMA	Methylmalonic acid
RDW	Red blood cell distribution width
RDX	Dextromethorphan
TIBC	Total iron binding capacity
TNT	Trinitrotoluene
UN	United Nations
WHO	The World Health Organization

INTRODUCTION

Relevance of the problem

Diseases of the blood-forming organs in children are currently an important problem of modern pediatrics, in particular anemia is one of the most common hematological disorders, which is recorded as detected in childhood. Thus, according to these literary sources, approximately a quarter of the Earth's population suffers from anemia, that is, almost 2 billion people, and almost half of them are children under 5 years of age [1, 2].

The significant prevalence of this disease among the pediatric population is probably due to the anatomical and physiological immaturity of the hematopoietic organs and their high sensitivity to the effects of negative environmental factors in childhood [3].

According to WHO experts, 1,62 billion people worldwide are susceptible to anemia (95% CI: 1,50–1,74 billion), which corresponds to 24,8% of the population (95% CI: 22,9–26,7%), while 47,4% are preschool children (95% CI: 45,7–49,1). At the same time, 20% of the world's population suffers from iron deficiency anemia (IDA), and its prevalence in young children is about 50,0% [4, 5].

Due to the high growth rate of the body, children, especially in the first year of life and during puberty (girls), are at risk of developing IDA. This is confirmed by data from WHO experts, according to which in children under five years of age, IDA is considered the most common deficiency state (DS) in the world and depends mainly on nutritional characteristics [6].

It should be noted that the higher prevalence of anemia is recorded in developing countries (51% in children under 4 years of age and 46% in children aged 5 to 12 years). However, young children are at risk of developing DS regardless of their place of residence, since their need for iron is high due to rapid growth, and its reserves in the body are insignificant [7]. According to statistics from the Ministry of Health of Ukraine, over the past five years, our country has observed a significant increase in IDA among children - 45–50% in children of the first three years and 21–29% in schoolchildren [8].

The problem of anemia in young children is of great social importance, since the development of the disease in this age group can lead to impaired physical development and metabolism. It is known that anemia leads to a decrease in the physical and emotional state of the child, causes sleep and appetite disorders, regardless of the cause, thus dramatically worsening the quality of life of young patients. At the same time, some forms of anemia pose a direct threat to the lives of babies, or are associated with a delay in the physical and sometimes mental development of the child [9].

There are many causes of anemia, both hereditary and acquired, and these causes vary greatly in populations around the world. Anemia itself is not a specific disease, but rather a heterogeneous group of pathological conditions [10].

The most common causes of anemia in children include children's nutrition, locality, and radiation pollution of the environment. Conflict-related environmental pollution, food security, health issues, bioterrorism, infectious disease risks, long-term hazards, psychological trauma, post-traumatic stress, reduced life expectancy, and other factors disrupt public health and have diverse manifestations, primarily in children [11-13]. The threat of negative feedback loops between conflict and public/environmental health is illustrated by the ongoing war between Ukraine and Russia.

Conflicts of the 21st century, unfortunately, are often accompanied by wars where women and children are not only the main victims, but also become targets of hostilities [7].

As sporadic bloodshed in Eastern Europe continues, international concern remains that this conflict has the real prospect of drawing the world into a new global crisis [14].

It is known that on February 24, 2022, Russia launched a full-scale military invasion of Ukraine, which was accompanied by missile and air strikes on residential buildings and medical facilities throughout Ukraine, as well as a significant ground invasion from several directions [15].

The first few months of the war were marked by attacks on military targets in Ukraine by Russian forces, particularly those near civilian residential areas. Attacks on ammunition depots, fuel tanks, and bombing of arsenals resulted in fires that released pollutants, heavy metals, and other ionizing substances into the air, affecting civilians and posing a threat to both local and regional air quality [16, 17].

A large body of evidence from numerous scientific literature sources has shown acute and chronic hazards associated with heavy metals arising from explosives, as well as energetic compounds such as trinitrotoluene (TNT), dextromethorphan (RDX), and rocket and missile propellants [18-21].

Documented evidence also shows that heavy metal pollution and aerosols cause numerous adverse effects on human health and the development of chronic diseases, and that their toxicity is a persistent problem for the environment due to their persistence and inability to degrade [22-25].

Therefore, the health of the Ukrainian population, as well as future generations, is under greater threat, as these dangers will persist long after the cessation of acute hostilities [26]. Research in this area is quite limited and somewhat controversial.

Thus, the purpose of the work is to analyze the features of the anemia in children of the Chernivtsi region before the start of the war in Ukraine and under martial law.

Research objectives:

1. To conduct a clinical and epidemiological analysis of the incidence of anemia among the child population in the pre-war period.
2. To assess the features of the course of anemia in children during martial law in Ukraine.

3. To conduct a comparative analysis of the features of the course of anemia in children before the war and during martial law.

Research object:anemia in children.

Subject of research:clinical and anamnestic data, results of assessment of clinical symptoms, data from laboratory examination of children with anemia.

Research methods: clinical (collection of complaints and anamnestic data, objective examination), general (indicators laboratory examination of children) mathematical (statistical processing of the obtained data on a personal computer in the program "STATISTICA® for Windows 7.0").

Approbation of results:

1. XII International Medical and Pharmaceutical Congress of Students and Young Scientists BIMCO 2025, 2-4 April 2-4, 2025, Chernivtsi. Report on the topic«ANEMIA IN CHILDREN". Speaker Abhibhawana.
2. Marusyk U.I., Abhibhawana ANEMIA IN CHILDREN . Colloquium-journal №44 (237), 2025. P.19-26.
3. Abhibhawana ANEMIA IN CHILDREN. Collection of materials of the Bukovina International Medical and Pharmaceutical Congress of Students and Young Scientists, BIMCO 2025, 2025. P.166.

Scientific novelty:

1. Extended clinical and epidemiological analysis of the incidence of anemia among children of Chernivtsi region in the pre-war period.
2. A comparative analysis of the features of the course of anemia among pediatric patients was conducted.before the start of hostilities and during the war in Ukraine.
3. For the first time, the clinical and epidemiological risks of the impact of military aggression on the development and course of anemia in childhood have been calculated.

THE MAIN PART

CHAPTER 1. LITERATURE REVIEW

1.1. Prevalence of anemia among the pediatric population and etiological factors of development

Anemia is one of the most common hematological pathologies in pediatric practice and is a significant public health problem, especially in developing countries. This disease is characterized by a decrease in the number of red blood cells or hemoglobin concentration, which disrupts the transport of oxygen to tissues and organs. Clinically, anemia is manifested by fatigue, pallor, weakness and growth retardation, which can negatively affect the child's cognitive development and quality of life [27, 28].

The global prevalence of anemia, especially iron deficiency anemia, remains extremely high and affects millions of children. Iron deficiency is the most common cause of anemia, which has serious health consequences, including impaired cognitive and physical development [29, 30]. In addition, hemolytic anemias, anemia of chronic disease, and hereditary hemoglobinopathies such as thalassemia and sickle cell anemia play a significant role [31-34]. Often, anemia is not only an independent condition, but also a symptom of other systemic pathologies that require careful examination.

Despite the availability of effective treatments, anemia often remains undiagnosed or untreated, especially in resource-limited settings [35]. Therefore, understanding the causes of anemia, diagnostic approaches, and treatment methods is an important step in reducing its burden among the pediatric population.

It is known that anemia is a pathological condition characterized by a decrease in hemoglobin and/or hematocrit levels below age-specific values, which depend on age, gender, and ethnicity.

The term "Anemia" comes from the Greek word meaning "without blood," meaning a decrease in hemoglobin concentration, red blood cell mass, or hematocrit in peripheral blood of >2 standard deviations below normal for the patient's age, sex, and ethnicity.

Simultaneously, studying the epidemiological indicators of anemia development in different countries provides important information regarding its prevalence, risk factors, and effectiveness of interventions [36].

Anemia is a global health problem affecting both low- and high-income countries, although the prevalence and causes vary considerably by region, level of health care, and economic conditions. The World Health Organization (WHO) estimates that anemia affects about 24,8% of the world's population, with the highest burden in low- and middle-income countries [37].

The highest prevalence of anemia is observed among children under 5 years of age and women of reproductive age. In children under 5 years of age, the global prevalence is about 42%, with the highest levels in sub-Saharan Africa, South Asia, and parts of Southeast Asia [37, 38].

The global prevalence of anemia among pregnant women is approximately 38%, with iron deficiency being the main cause. In low-income countries, women are more likely to suffer from anemia due to poor nutrition, high fertility rates, and limited access to iron-rich foods or supplements.

The overall prevalence of anemia in Ukraine is estimated at approximately 20% of cases, with higher rates observed among children and pregnant women.

Instead, in India the high prevalence of anemia is recorded at 69,2% among children aged 6–59 months and 53% among women of reproductive age. The main causes of the development of this disease in both countries are similar and include iron deficiency, anemia of chronic diseases, chronic infections and probable malnutrition.

Regarding the prevalence of anemia in the world,on average, 24,8% of the population suffers from anemia, with the highest rates among children, pregnant women, and those with chronic health problems.

Anemia in childhood is a multifactorial condition that is caused by many factors, including age, gender, heredity, environmental influences, nutrition, and the use of various medications [37, 39].

Age is a key factor in the development of anemia, as its causes and prevalence change at different stages of childhood development. Physiological needs for iron and other nutrients change with age, which affects the risk of developing anemia.

During the first six months of life, infants are usually protected from anemia by the stores of iron and other trace elements accumulated during intrauterine development. However, at about 6 months, these stores are depleted, and the risk of iron deficiency anemia increases significantly, especially in cases where the infant is not breastfed or the nursing mother does not consume iron-fortified foods [31, 32]. Iron deficiency anemia is particularly common in this age group. Additional risk factors for anemia in infants include neonatal jaundice and hemolytic diseases [40]. Premature infants are at particular risk, as they have fewer iron stores at birth.

At the same time, in preschool age (1–5 years)the need for iron increases due to intensive physical development. The main cause of anemia remains iron deficiency in the child's body, which is caused by insufficient consumption of meat, legumes and cereals, or excessive consumption of cow's milk, which impairs iron absorption. At this age, children may also develop hereditary hemoglobinopathies (sickle cell anemia, thalassemia), especially in regions with a high prevalence of these conditions among the population [31-34].

During adolescence (10–18 years)anemia often occurs due to the body's increased need for iron, especially in girls due to the onset of menstruation. Heavy or irregular menstrual bleeding can lead to significant iron loss. Another common cause of anemia in adolescents is an unbalanced diet, in particular, teenage girls often switch to a specific diet (vegetarian or vegan diets), the products consumed in such a diet may be poor in bioavailable iron, vitamin B_{12}, or folic acid [41].

Simultaneously,the prevalence and types of anemia in childhood are significantly influenced by gender differences, which are caused by both biological and behavioral factors.

So, during adolescence, girls are more likely to suffer from anemia due to menstruation and the associated blood loss. Heavy menstrual bleeding can cause iron deficiency anemia [42]. In addition, inadequate dietary iron intake is common at this age. Teenage pregnancy also increases the risk of anemia due to the increased need for iron and folic acid [42, 43].

In return, boys are less likely to suffer from anemia associated with blood loss, but may suffer from iron deficiency, hereditary hemoglobinopathies, or chronic diseases.

The presence of hereditary hemoglobinopathies and genetic blood diseases such as thalassemia and sickle cell anemia significantly increases the risk of developing anemia.

Thalassemia – a recessive autosomal disease that causes impaired hemoglobin synthesis. It is known that heterozygous carriers develop a mild form of anemia (thalassemia minor), while homozygous carriers develop a severe form (thalassemia major), which requires regular blood transfusions [33, 34].

Sickle cell anemia – a genetic disorder in which abnormal hemoglobin (HbS) is formed, which causes a change in the shape of red blood cells, disrupting their functioning, causing their hemolysis, the development of chronic anemia, and vaso-occlusive crises [33].

Thus, thalassemia and sickle cell anemia are hereditary spherocytosis that have a genetic nature. These pathologies cause the development of chronic anemia due to defective hemoglobin synthesis or increased destruction of erythrocytes.

Important exogenous factors for the development of anemia in children include the influence of infections, toxins, and adverse living conditions.

So, parasitic diseases, particularly malaria and helminthiasis (hookworm, schistosomiasis), are the leading causes of anemia in tropical and subtropical regions. Malaria, caused by Plasmodiumspp, leads to the destruction of red blood cells and causes acute or chronic anemia. Helminths cause chronic blood loss through the intestinal mucosa, which leads to iron deficiency in the body.

In cities, especially in older buildings, or where there are contaminated water sources, exposure to lead can inhibit hemoglobin synthesis and cause microcytic anemia. Lead poisoning is also associated with cognitive impairment in children.

Lack of access to clean water and proper hygiene increases the risk of infections, malnutrition and, as a result, the development of iron deficiency anemia [44].

According to literature data, pation is one of the key modifiable risk factors for anemia in children. The most common causes of anemia in childhood are iron, vitamin B_{12}, and folic acid deficiencies. Iron deficiency as a cause of anemia was first discovered in 1852 by Karl Fiordt and his student G. Welcher. Over the next century, the mechanisms of iron regulation in the body were studied in detail [45].

The main factor iron deficiency in the body is insufficient consumption of foods rich in bioavailable iron, in particular meat, fish and poultry. Children whose diet is based mainly on plant foods without sources of iron (e.g. legumes, cereals, dark green vegetables) have a higher risk of developing anemia according to the literature [43, 44].

Vitamin B_{12} and folic acid deficiency withit is mainly observed when there is insufficient consumption of animal products. This is especially true for children who follow a vegetarian or vegan diet.

Lack of a balanced diet due to poverty, lack of access to quality food, or food insecurity increases the risk of developing both iron deficiency and megaloblastic anemia in childhood [43, 44].

We should not forget that some medications can disrupt erythropoiesis or cause hemolysis, leading to the development of anemia.

1.2. Pathophysiological and clinical features of anemia in children

It is known that anemia develops due to an imbalance between the production, destruction, or loss of red blood cells, which disrupts the body's ability to provide tissues with sufficient oxygen.

Reduced red blood cell production – the most common mechanism of anemia is a deficiency of nutrients such as iron, folic acid, or vitamin B_{12}. These components are critical for the synthesis of hemoglobin and DNA in erythropoiesis precursor cells. However, bone marrow dysfunction, particularly in aplastic anemia or tumor infiltration, can also lead to inhibition of erythropoiesis [46].

Increased destruction of red blood cells (hemolysis)occurs when the lifespan of red blood cells is shortened. This phenomenon may be associated with intrinsic defects, such as sickle cell anemia, hereditary spherocytosis, or glucose-6-phosphate dehydrogenase (G6PD) deficiency. Such pathological changes sometimes disrupt the structure, membrane, or enzymatic processes in red blood cells, leading to their premature destruction.

Acute (trauma, surgery) or chronic blood loss (gastrointestinal bleeding, menorrhagia) leads to a decrease in the number of red blood cells and iron stores. In chronic losses, iron does not have time to replenish, which causes secondary iron deficiency [47, 48].

In chronic inflammation (infections, autoimmune conditions, cancer, renal failure), the cytokine interleukin-6 is produced, which stimulates an increase in hepcidin levels. Hepcidin blocks the release of iron from macrophages and inhibits its absorption in the intestine, which reduces the availability of iron for erythropoiesis.

According to literature sources, anemia has both common and age-specific clinical manifestations, which are due to physiological characteristics, adaptive mechanisms, and dominant etiological factors.

In children, anemia often manifests itself with nonspecific signs, including:

- irritability, drowsiness;
- rapid fatigue, weakness;
- poor appetite and refusal to feed in infants;

- delayed physical growth and psychomotor development;
- paleness of the skin and mucous membranes;
- tachycardia, reduced physical activity;
- in severe cases - "physical development delay", or the so-called "failure to thrive syndrome";
- Schoolchildren have difficulty concentrating and decreased academic performance.

Some specific forms of anemia have additional manifestations:

- **iron deficiency anemia:** may be accompanied by the appearance of a craving for eating inedible substances
- **hemolytic anemia:** may manifest as jaundice, due to massive destruction of red blood cells and release of bilirubin, and enlargement of the spleen (splenomegaly).

In adulthood, anemia usually manifests itself in the following common symptoms:

- general weakness, lethargy;
- shortness of breath during physical exertion;
- pale skin;
- rapid heartbeat (tachycardia);
- dizziness, feeling of "unsteadiness", especially when changing body position;
- decreased tolerance to physical activity.

In severe cases, the following may occur:

- chest pain (especially in patients with cardiovascular disease);
- cognitive impairment, difficulty concentrating;
- glossitis (inflammation of the tongue), angular stomatitis (cracks in the corners of the mouth) - often with B_{12} or folic acid deficiency;
- paresthesias (tingling sensation) - characteristic of anemias associated with vitamin B_{12} deficiency.

Anemias are classified according to various criteria, which allows us to better understand the pathogenesis and choose the optimal treatment tactics.

1. According to the etiological principle, the following are distinguished:

- Intraerythrocytic (congenital):
  - caused by genetic disorders of the structure or metabolism of erythrocytes.
- Extraerythrocytic (acquired):
  - caused by external influences, infections, nutrient deficiencies, or systemic diseases.

2. By severity (based on hemoglobin level):

- Norm:≥120 g/l
- Mild anemia:>90 g/l
- Moderate anemia:70–90 g/l
- Severe anemia:<70 g/l
- Very severe anemia:<50 g/l

3. By erythrocyte morphology (by mean corpuscular volume — MCV):

- Microcytic:mean diameter <6.7 μm, MCV <80 fl
- Normocytic:average diameter 7–8 μm, MCV 80–100 fl
- Macrocytic:average diameter >8 μm, MCV >100 fl

4. By the number of reticulocytes (assessment of the regenerative function of the bone marrow):

- Hyporegenerative:< 0.2%
- Normoregenerative:0.2–1.2%
- Hyperregenerative:>1.2%

5. According to clinical and pathogenetic features:

A. Anemias caused by blood loss:

- Acute posthemorrhagic anemia

- Chronic posthemorrhagic anemia

B. Anemias caused by impaired hematopoiesis:

a. Disorders of hemoglobin synthesis:

- iron deficiency anemia
- anemia caused by iron redistribution (in infections, inflammation)
- anemias associated with impaired porphyrin synthesis
- anemias associated with a defect in heme or globin synthesis

b. Disruption of DNA and RNA synthesis: megaloblastic anemias (B_{12}, folic acid deficiency)

c. Dyserythropoietic anemias**:** associated with a violation of the process of division of erythroid cells

d. Inhibition of bone marrow cell proliferation (for example, in aplastic anemia)

d. Replacement of hematopoietic bone marrow tissue with tumor cells

e. Disturbance of erythropoietin production or the action of its inhibitors

C. Anemias caused by increased destruction of erythrocytes (hemolytic):

1. Hereditary hemolytic anemias:

- membranopathies
- enzymeopathies
- hemoglobinopathies

2. Acquired hemolytic anemias

1.3. Features of diagnosis, treatment and prevention of anemia in children

Physical examination remains a fundamental element in the clinical evaluation of anemia. It provides valuable information about the severity, possible etiology, and systemic effects of anemia. A systematic approach increases diagnostic accuracy and helps guide further laboratory testing.

The first stage of the examination involves examining the child's general appearance, assessing the level of activity and development for age. Pale skin is a classic sign of anemia, most informative when examining the conjunctiva, nail beds, palms and oral mucosa. Studies show that conjunctival pallor is moderately correlated with hemoglobin levels, especially in moderate and severe anemia [49, 50].

Tachycardia and a hyperdynamic pulse may be compensatory responses to decreased oxygen delivery. In severe anemia, orthostatic hypotension and systolic murmurs may occur due to decreased blood viscosity and increased cardiac output.

Specific systemic findings include the following changes on examination:

1. Skin and nails:

- Pallor, an extremely informative sign provided that the examination is performed in anatomically appropriate areas.
- Koilonychia (spoon-shaped nails), a sign characteristic of chronic iron deficiency.
- Jaundice indicates hemolysis, typically in hemolytic anemias.
- Petechiae, ecchymoses may indicate thrombocytopenia or hematopoietic suppression.

2. Head and neck:

- Glossitis, angular stomatitis –typical signs of vitamin B_{12} or folic acid deficiency.
- Lymphadenopathy possible with chronic infections or malignant diseases.
- Pallor of the conjunctiva –validated sign of anemia.

3.Abdominal cavity:

- Hepatosplenomegaly characteristic of hemolytic anemias and metabolic disorders.
- Asymmetries, ascites may indicate anemia due to liver disease.

4. Neurological examination:

- Paresthesia, ataxia: typical manifestations of vitamin B_{12} deficiency (subacute combined degeneration of the spinal cord).
- Developmental delay: common in chronic iron deficiency in children.

Laboratory studies are necessary to confirm the diagnosis of anemia, assess its severity, and determine the underlying etiology. A sequential approach that begins with basic tests and progresses to more specialized tests based on clinical symptoms provides an accurate and cost-effective diagnosis [51]. Laboratory tests used to diagnose anemia can be divided into the following positions.

1. Initial screening tests:

Complete blood count (CBC):The CBC is the primary method for assessing anemia and provides critically important information:

- Hemoglobin (Hb):determines the presence and degree of anemia based on age and gender norms.
- Hematocrit (Hct):reflects the volume fraction of erythrocytes in the blood.
- Erythrocyte indices:
  - Mean corpuscular volume (MCV):allows classification of anemia as microcytic (<80 fl), normocytic (80–100 fl), or macrocytic (>100 fl).
  - Mean corpuscular hemoglobin (MCH)and mean corpuscular hemoglobin concentration (MCHC): help identify hypochromia or normochromia.
  - Red blood cell distribution width (RDW): allows you to distinguish between homogeneous (low RDW) and heterogeneous (high RDW) erythrocyte sizes, which is important in combined anemias.

Reticulocyte count:this indicator reflects the production of new red blood cells by the bone marrow. A high level of reticulocytes indicates an adequate bone marrow response, often seen in hemolysis or acute blood loss, while a low level indicates bone marrow suppression or insufficient erythropoiesis.

2. Iron metabolism study:

Iron deficiency anemia , or iron deficiency anemia, is the most common cause of anemia worldwide. Key tests include:

- Serum ferritin, whichreflects iron stores in the body; a low level of ferritin confirms IDA. It should be borne in mind that ferritin is an acute phase protein, therefore, in inflammatory processes of various genesis, its level may be falsely elevated.
- Serum iron:decreased in IDA, but may also be decreased in anemia of chronic disease.
- Total iron binding capacity (TIBC):usually increases in IDA due to increased transferrin production.
- Transferrin saturation:calculated based on serum iron and TIBC; low levels are characteristic of IDA.

3. Vitamin and nutrient levels:

- Deficiencies in vitamin B_{12} and folic acid levels lead to macrocytic anemia, and B_{12} deficiency is also associated with neurological symptoms.
- Homocysteine and methylmalonic acid (MMA): elevated levels of both markers indicate vitamin B12 deficiency, while isolated elevation of homocysteine indicates folate deficiency.

4. Hemolysis tests:

- Peripheral blood smear:allows you to detect abnormal morphological changes in red blood cells, such as spherocytes (hereditary spherocytosis) or sickle cells (sickle cell anemia).
- Lactate dehydrogenase (LDH):increases during hemolysis due to destruction of erythrocytes.
- Haptoglobin:decreases in hemolytic anemia because it binds to free hemoglobin in plasma.
- Indirect bilirubinemia:increases due to the breakdown of erythrocytes.

- Direct Coombs test:allows you to diagnose autoimmune hemolytic anemia.

5. Specialized tests:

- Hemoglobin electrophoresis:used to detect hemoglobinopathies such as sickle cell anemia or thalassemia.
- Bone marrow aspiration and biopsy:performed in cases of suspected bone marrow involvement, particularly aplastic anemia or leukemia.
- Genetic testing:allows you to confirm the diagnosis of hereditary anemias, such as thalassemias or enzyme pathologies (for example, G6PD deficiency).

6. Studies in anemia of chronic diseases:

- C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR):inflammation markers.
- Hepcidin level:increases in chronic inflammatory processes, which inhibits the mobilization of iron from stores and reduces its absorption in the intestines.

History, physical examination, and initial laboratory tests are used to narrow the diagnostic search and determine the need for additional tests.

- Abnormalities of other cell lines.The first step in narrowing down the diagnostic options is to determine whether the patient has isolated anemia or whether abnormalities in other cell lines are also present.
- Pancytopenia.Causes of pancytopenia in children may include infections, myelosuppressive drugs, leukemia, aplastic anemia, and hypersplenism.
- Anemia with thrombocytopenia.Causes of anemia in combination with low platelet counts include hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, and Evans syndrome. In rare cases, children with severe iron deficiency anemia may also have thrombocytopenia.

- Anemia with thrombocytosis.Iron deficiency anemia is often accompanied by thrombocytosis, although it can also manifest as thrombocytopenia.
- Anemia with leukocytosis.Causes of anemia combined with elevated white blood cell levels may include leukemia or infections.

After narrowing the diagnostic search based on MCV (mean corpuscular volume) and reticulocyte level, confirmatory tests are performed.

- If hemolytic anemia is suspected, a direct Coombs test, indirect bilirubin, lactate dehydrogenase (LDH), and haptoglobin levels should be obtained. Testing for specific etiologies may include a Coombs test, a screening test for glucose-6-phosphate dehydrogenase (G6PD) deficiency, osmotic fragility, and/or hemoglobin electrophoresis.
- If iron deficiency is suspected, additional testing may include an assessment of iron metabolism (e.g., serum ferritin). Iron testing is not necessary in children < 2 years of age who have mild microcytic anemia and a consistent dietary history. In such cases, a therapeutic iron challenge can be used to confirm the diagnosis.
- Testing for other nutritional deficiencies and/or lead poisoning may include measuring folate, vitamin B_{12}, and lead levels in the blood.
- Bone marrow aspiration or biopsy may be necessary to evaluate for leukemia or other causes of bone marrow suppression (e.g., aplastic anemia, Diamond-Blackfan anemia).

According to the literature, the treatment of anemia involves identifying and eliminating the underlying cause, correcting the hemoglobin deficiency, and preventing recurrence [8, 50, 51]. A structured approach ensures effective therapy adapted to the etiology, severity of the condition, and individual patient characteristics such as age, comorbidities, and nutritional status.

The first step in treating anemia is to stabilize the patient, especially in severe anemia that compromises oxygen delivery to the brain. Hemodynamic instability, or critical hemoglobin levels (<7 g/dL in most cases), may require red blood cell transfusions to rapidly restore the oxygen-carrying capacity of the blood. In non-emergency cases, treatment focuses on correcting the deficiency and the underlying cause of the anemia [50, 51].

Treatment of so-called nutritional anemias, i.e. those associated with nutritional problems in the child, depends on the type of deficiency that the patient has. Thus, treatment of IDA involves oral administration of iron preparations (sulfate, ferrous gluconate) in cases of mild to moderate severity. Typical dosage is 3–6 mg/kg/day for children, or 150–200 mg/day for adults. Parenteral administration of iron (e.g., iron carboxymaltose, iron sucrose) is used in patients with intolerance to oral forms, severe deficiency or malabsorption syndromes. Rational dietary changes include increasing the consumption of foods rich in iron (e.g., red meat, dark green vegetables) and vitamin C to improve absorption [8, 9].

In case of B_{12} deficiency, intramuscular administration of cyanocobalamin or hydroxocobalamin (1000 mcg daily for 1 week, then weekly for a month, and then monthly) is preferred, followed by a switch to oral forms. Folate deficiency is treated with oral folic acid 1–5 mg/day. In cases of combined deficiency, vitamin B_{12} deficiency must be corrected first to avoid neurological complications [8].

In the case of hemolytic anemia, treatment depends on the etiology of the disease:

- Immune hemolysis:treated with glucocorticoids, intravenous immunoglobulin (IVIG) or immunosuppressants. In resistant cases, splenectomy may be indicated.
- Sickle cell anemia:hydroxycarbamide is the main drug to reduce the frequency of vaso-occlusive crises, and folic acid is also prescribed. Transfusions and exchange transfusions are used in acute crises or severe anemia. Bone marrow transplantation is a potentially radical treatment in selected patients [10].
- G6PD deficiency:treatment consists of avoiding oxidative triggers (certain medications, beans), as well as symptomatic support during episodes of hemolysis.

Treatment of anemia like chronic diseases focuses on the therapy of the underlying disease (infection, inflammatory process of any origin, malignant processes). In severe cases, erythropoiesis stimulants (erythropoietin or darbepoetin) are used, especially in chronic kidney disease, usually in combination with iron preparations to achieve an adequate response [9].

Severe aplastic anemia is treated with immunosuppressive therapy (antithymocyte globulin combined with cyclosporine) and hematopoietic stem cell transplantation (HSCT) in eligible patients. Supportive treatment includes blood transfusions and infection prevention [9, 10].

Prevention of recurrence involves addressing nutritional deficiencies through public health interventions such as fortification of staple foods with iron and folic acid, deworming programs in endemic areas, and improved access to prenatal care. Regular monitoring and patient education on nutrition and adherence to treatment are important components of long-term anemia control.

1.4. The impact of war on the development of various diseases in children

Three years into Russia’s full-scale military invasion of Ukraine, a crisis has emerged and is growing in scale. The escalation of the conflict in Ukraine has resulted in numerous civilian casualties, forcing people to flee their homes in search of safety and protection.

The war in Ukraine has already resulted in thousands of deaths and millions of refugees, creating one of Europe's largest humanitarian crises since World War II.

Thus, according to the UN, since the beginning of the invasion, the organization has recorded and confirmed data on 12,654 dead and 29,392 injured civilians in Ukraine. Among them, as the data shows, 673 children were killed, 1,865 were injured. According to the UN, from February 2022 to February 2025, at least 790 Russian attacks were recorded that damaged or destroyed medical facilities, and 1,670 attacks on educational institutions [52].

At the same time, as of November 30. 2024 4,2 million Ukrainians had temporary protection status in the countries of the European Union, testify Eurostat data. Among people with temporary protection status, adult women accounted for almost half (44,9%) of beneficiaries, and children accounted for almost a third (32,0%) of the total [53]. In addition, over 5,4 million people remain internally displaced [54, 55]. The war contributes to the spread of disease among refugees and is likely to cause new outbreaks of infectious diseases such as tuberculosis, sexually transmitted infections, and diarrheal diseases [56-59].

The first few months of the crisis were marked by attacks on military targets in Ukraine by Russian forces, particularly those near civilian residential areas [60, 61]. Attacks on ammunition depots, fuel tanks, and bombing of arsenals resulted in fires that released pollutants, heavy metals, and other ionizing substances into the air, affecting the civilian population [16, 17].

According to literature data, heavy metal pollution and aerosols cause numerous harmful and chronic effects on human health, and that their toxicity is a constant problem for the environment due to their persistence and inability to decompose [22-25].

Meanwhile, nearly 100,000 people were left without water supplies before the invasion due to the destruction of water bodies [61, 62]. Various United Nations (UN) agencies and humanitarian organizations have documented the widespread destruction of water bodies during the ongoing war. The World Health Organization (WHO) has warned that this situation could lead to environmental problems related to the spread of infectious diseases due to the lack of clean drinking water [63].

The ongoing war also threatens four nuclear facilities in Ukraine. The capture of the Chernobyl nuclear power plant by Russian troops has sparked international concern, as radiation levels have increased due to the movement of troops in the exclusion zone.

Scientists estimate that 2 to 3% of all deaths worldwide can be attributed to intercontinental conflicts, including conflict-related injuries. Therefore, the importance of epidemiological analysis to identify the underlying causes and reduce the likelihood of death from these factors is of paramount importance.

The health impact of war is not limited to direct casualties from combat. Researchers estimate that for every life lost to war, nine are lost indirectly, although this estimate varies depending on the scale of the crisis and the underlying health conditions in the countries involved in the conflict [64].

War mutilates the environment and disrupts its aesthetics. The current war in Ukraine is accompanied by deliberate attacks on civilian infrastructure and health, which negatively affects the provision of medical care due to the lack of access to medical facilities for both medical workers and patients, as well as the difficulty of transporting vital medical supplies [65].

Health outcomes, especially among pregnant women and infants, will deteriorate rapidly, as child and maternal mortality is known to be significantly higher during armed conflict. [66] The physical and mental health challenges experienced by millions of refugees and internally displaced persons will be significant, and the physical and psychological trauma experienced by millions in Ukraine will be felt long after this conflict ends [67].

Thus, the war in Ukraine, which has been going on for more than three years, significantly increases the risks of anemia in children both in front-line zones and in the so-called safe regions of the country.

CHAPTER 2

MATERIAL AND RESEARCH METHODS

2.1. General characteristics of patients

To achieve 113 medical records of children who were hospitalized in the Chernivtsi Regional Children's Hospital (CRCH) for anemia from 2020 to 2024.

In the cohort of 113 patients, there were 52 boys (46,0%) and 61 girls (54,0%), of whom 67 (59,3%) were urban residents, and 46 children (40,7%) were rural residents. Among the children whose medical records were included in the analysis, 89 (78,7%) attended preschool institutions and school and 24 children (21,3%) were unorganized. By the social status of the parents, the surveyed families were divided as follows: both parents work 31%, the father does not work - 30%, the mother does not work – 14,4%, both parents are unemployed – 19,6%, and 5% were orphans or half-orphans.

At the same time, 8% of patients are internally displaced persons due to the war in Ukraine.

Based on the time of hospitalization, the cohort of children was divided into two clinical comparison groups. The first (I) was formed by 67 patients who were hospitalized in the CRCH for anemia during the war, namely 2022-2024, and the second (II) comparison group included 46 children in whom anemia was diagnosed and the patients were inpatients in the pre-war years (2020-2022). The formed groups were comparable in terms of the main clinical characteristics (Table 2.1).

Table 2.1

General characteristics of comparison groups (%)

Clinical groups	Number of children	Sex		Place residence		Organized	Disorganized
		Boys	Girls	City	Village		
Group I	67	41,8	58,2	32,8	67,2	76,0	24,0
Group II	46	52,3	47,7	45,7	54,3	82,6	17,4
Pt		> 0,05	>0,05	> 0,05	> 0,05	> 0,05	> 0,05

According to the social status of the parents, the surveyed families were divided into groups as follows: in clinical group I, the share of both parents working was 31,6%, the father was unemployed – 19,3%, the mother was unemployed – 10,5%, both parents were unemployed – 22,8%, and 15,5% were orphans or halforphans. In clinical group II, these figures were 20,0%, 33,0%, 4,0%, 35,6%, and 7,4%, respectively (in all cases, $P\varphi>0,05$).

The age of children at the time of hospitalization did not differ between the groups: in the I clinical group the average age was 9,2±5,53 years, in children hospitalized with anemia in the pre-war period – 9,9±5,76 years ($P\varphi>0,05$). The duration of the disease was on average 2,1±3,9 years in children who were hospitalized during the Russian military aggression against Ukraine and 3,1±4,7 years in patients of the comparison group ($P\varphi>0,05$).

2.2. Objective research methods

During the study, anamnestic data of pediatric patients with anemia were evaluated. Clinical data were analyzed taking into account the availability and expressiveness of data from objective examination of patients. In clinical comparison groups, data from laboratory research methods were also evaluated, in particular, changes in the general blood test specific for this disease.

The study conducted a comparative analysis of clinical, anamnestic and laboratory data in two different time periods — during the war in Ukraine (group I) and before the start of hostilities (group II).

2.3. Statistical analysis methods

The obtained results of the study were analyzed using the computer packages "STATISTICA" StatSoft Inc. and Excel XP for Windows on a personal computer using parametric and nonparametric calculation methods. The validity of the null hypothesis was determined taking into account the significance level "P". To assess the features of the course of anemia, quantitative data in groups were compared using the Student's t-test (in the case of normal distribution) or nonparametric methods (in the case of deviation from normality). The data are presented as M ± SD (mean ± standard deviation). Differences were considered statistically significant at $p < 0,05$.

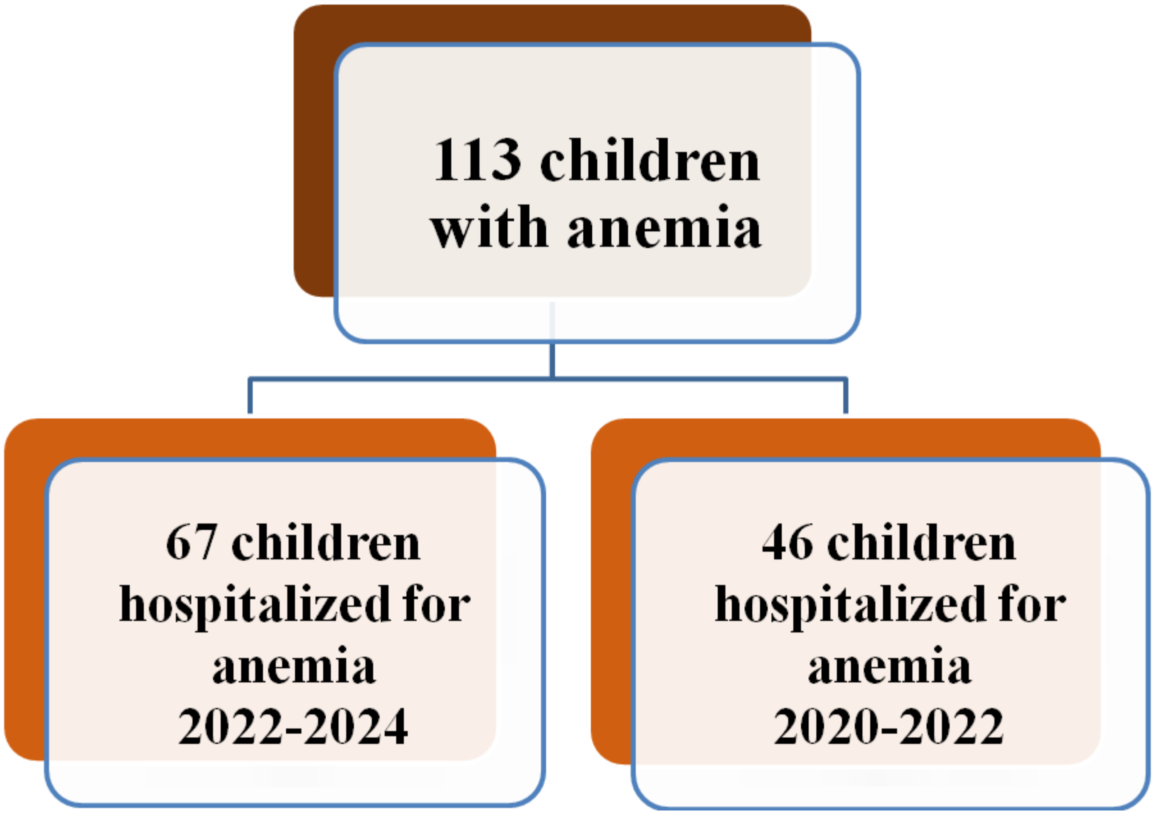
The risk assessment of the event was carried out taking into account the probability of the values of relative (RR), attributive (AR) risks and odds ratio (OR), as well as the determination of their confidence intervals (95% CI) [68-70].

2.4. Ensuring bioethical requirements

This study was conducted taking into account the basic provisions of GCP ICH and the Declaration of Helsinki on biomedical research, where a person is their object, which provided for compliance with the concept of informed consent, consideration of the benefits over the risk of harm, the principle of confidentiality and respect for the child's personality as a person incapable of self-protection, and other ethical principles regarding children who are the objects of research.

The work was carried out at the Department of Pediatrics and Children's Infectious Diseases (Head - Prof. Koloskova O.K.) of the Bukovinian State Medical University (Rector - Prof. Gerush I.V.).

2.5. Research design



CHAPTER 3
GENERAL CHARACTERISTICS OF THE FEATURES OF THE COURSE OF ANEMIA IN CHILDHOOD PATIENTS.

3.1. Clinical and epidemiological profile of children with anemia

As part of the study of clinical and epidemiological features of children with anemia, the age distribution, duration of hospitalization, duration of the disease and reproductive history of mothers were analyzed. The obtained data allow us to characterize the epidemiological aspects of anemia in the studied cohort of children for their further distribution into groups (main, control).

The average age of children included in the study was 13,6 ± 1,88 years. The study analyzed the age distribution of children who were hospitalized in the hematology department with various clinical manifestations of anemia (Fig. 3.1). In general, the sample included patients aged 1 month to 18 years. In the group of children from 1 month to 1 year, 9 cases were registered. In the age interval from 1 to 3 years - 17 children, from 3 to 6 years - 16 children. The largest number of hospitalized patients was observed in the age groups from 6 to 11 years and from 14 to 18 years - 23 and 26 cases, respectively. The age group 11–14 years included 22 children. The data obtained indicate an uneven distribution of the frequency of hospitalizations with anemia among children of different ages, with a predominance in older age groups. The most numerous groups of children were those aged 14–18 and 6–11.

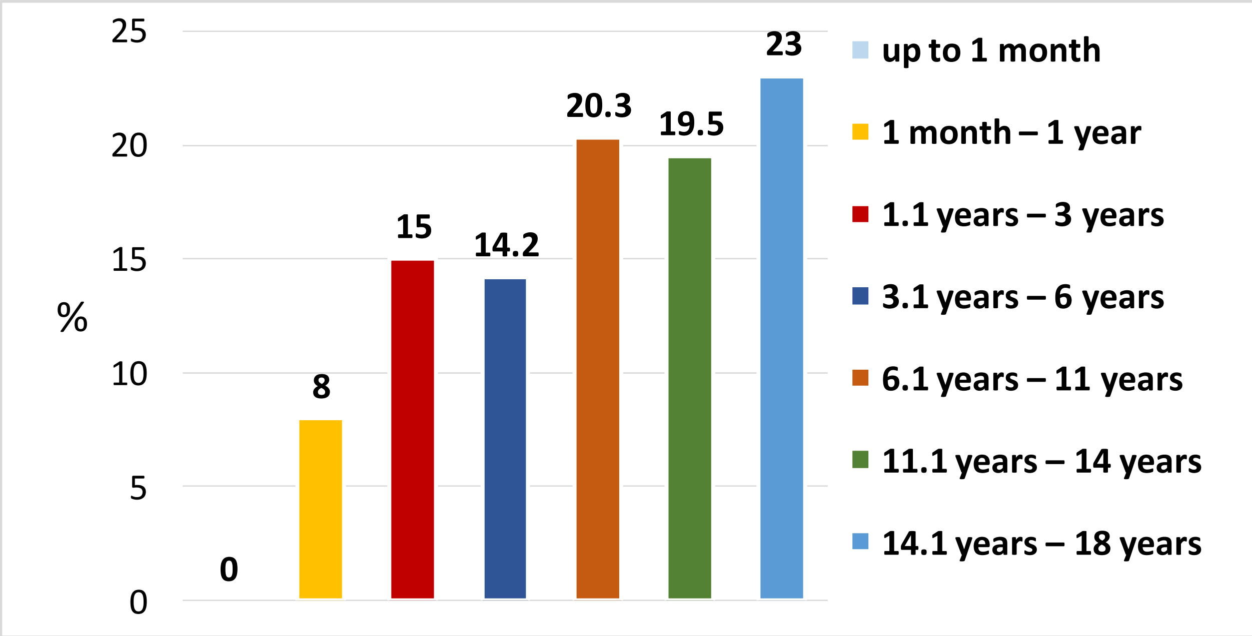


Fig. 3.1. Distribution by age groups

This distribution may reflect an increased frequency of anemia detection in adolescence, possibly due to physiological characteristics (rapid growth, hormonal changes), or malnutrition, as well as in primary school age, which may be associated with an increased risk of deficiency states.

Analysis of the distribution of young patients by family social status (Fig. 3.2) revealed significant variability in socio-economic background, which could potentially affect both the risk of anemia and access to medical care. Only 27 children had parents who were officially employed, which can be regarded as socially prosperous conditions. The remaining patients showed signs of socially vulnerable situations: in 26 children the father did not work, in 8 children the mother did not work, and in 17 cases both parents were not employed, which indicates a significant level of social maladjustment of families. Orphans and half-orphans are a particularly vulnerable category - 9 people, who, as a rule, have limited access to full nutrition, preventive medical examinations and proper care.

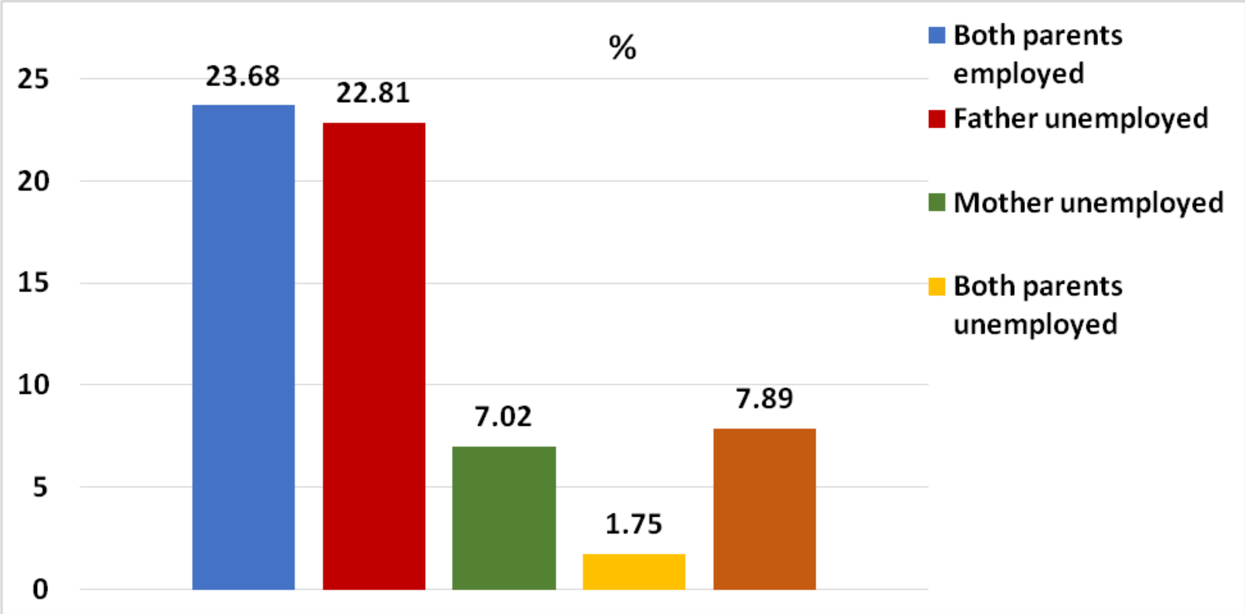


Fig. 3.2. Analysis of the social status of the parents of the examined patients

In total, 76,32% of cases, children came from families with at least one of the factors of social disadvantage - unemployment of one or both parents, or lack of parental care. Such conditions can contribute not only to the late detection of anemic conditions, but also to an increased risk of developing severe forms of anemia due to the long-term impact of factors such as unbalanced nutrition, household neglect, and low medical awareness of parents.

A comprehensive analysis of the family and parental history of children with anemia allows us to partially outline the possible role of hereditary factors in the development of the disease. In most cases, the family history was unencumbered — there were 83 such children, which indicates the absence of identified genetic or hereditary factors in the families of patients. At the same time, 30 children had a burdened family history, which potentially indicates a genetic predisposition to blood system disorders or concomitant somatic pathology that may affect the development of anemia.

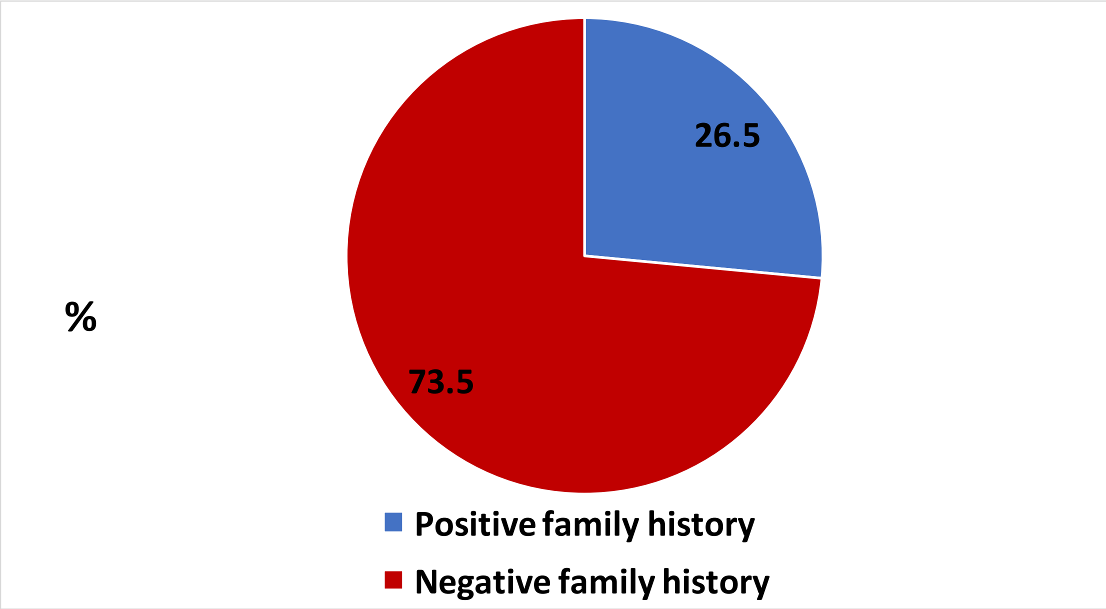


Fig. 3.3. Analysis of the number of children with a complicated family history

In general, the presence of a burdened family history in almost a fifth of cases requires further targeted research, however, the significant amount of missing data does not allow for unambiguous conclusions regarding the degree of influence of heredity on the etiology of anemia in this sample.

Analysis of the distribution of hospitalized children by internally displaced person (IDP) status (Fig. 3.4) showed that the absolute majority of patients — 104 people — did not have IDP status, while only 9 cases had children belonging to this category. Thus, the share of internally displaced persons among the surveyed sample is minimal.

The low percentage of IDP children in the hematology hospital structure may be due to several factors. On the one hand, this may indicate limited access of IDPs to specialized medical care due to logistical, social or economic barriers. On the other hand, it is also possible that the study region is dominated by local patients, and the share of displaced people among the total child population is relatively small. It is also worth considering that IDPs may apply to medical institutions of other profiles or live in places with insufficient access to hematology care.

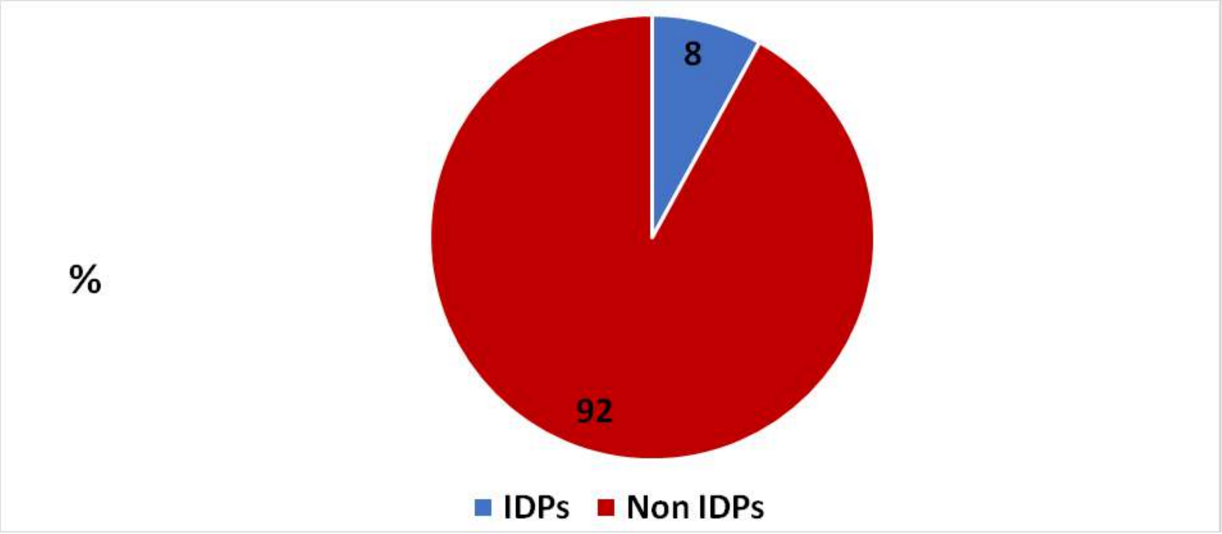


Fig. 3.4. Analysis of the number of children by Internally Displaced Person (IDP) status

Despite the small representation of IDPs in this sample, it is advisable to take into account the potential medical and social risks of this group, in particular the impact of stress, malnutrition, and loss of a permanent source of medical supervision, which may contribute to the development or exacerbation of anemic conditions in children.

Analysis of the obstetric history of patients (Fig. 3.5) shows that in most cases it was uncomplicated, i.e. no complications were recorded during pregnancy, childbirth or the perinatal period that could have an impact on the subsequent somatic condition of the child. Only in 3 cases was a complicated obstetric history revealed, which indicates a relatively low proportion of children who potentially had an increased risk of developing diseases caused by adverse prenatal or natal factors.

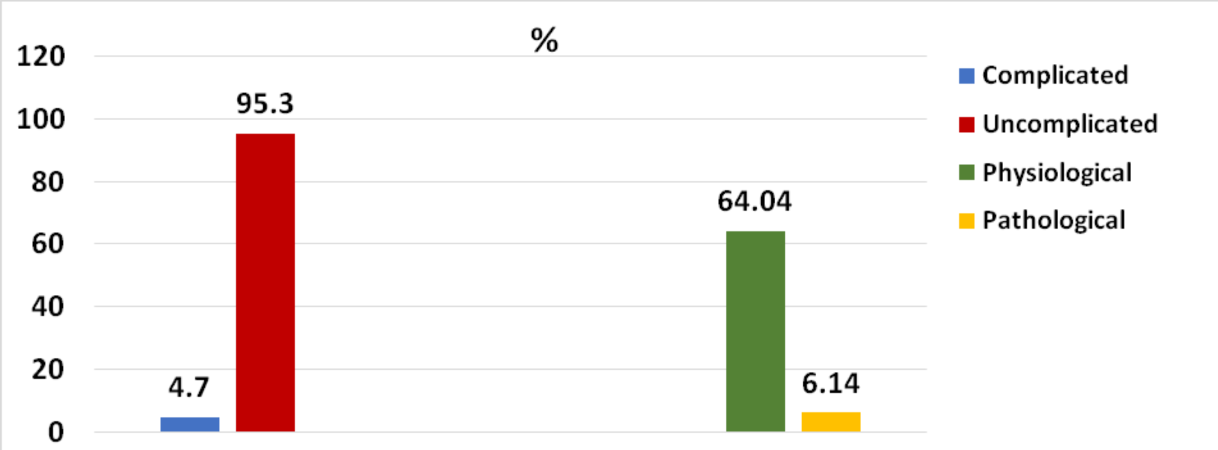


Fig. 3.5. Analysis of obstetric history

Note: Legend – 1: Course of pregnancy, 2: Course of delivery.

Thus, the total indicators of uncomplicated pregnancy and physiological childbirth indicate that the majority of children hospitalized with anemia did not have a significant obstetric background that could be considered a risk factor.

Analysis of data on the order of pregnancy (Fig. 3.6) from which hospitalized children were born revealed that the largest proportion was children born as a result of the first pregnancy — 35 people. 24 children were born from the second pregnancy, and 20 patients were born as a result of the third or subsequent pregnancies.

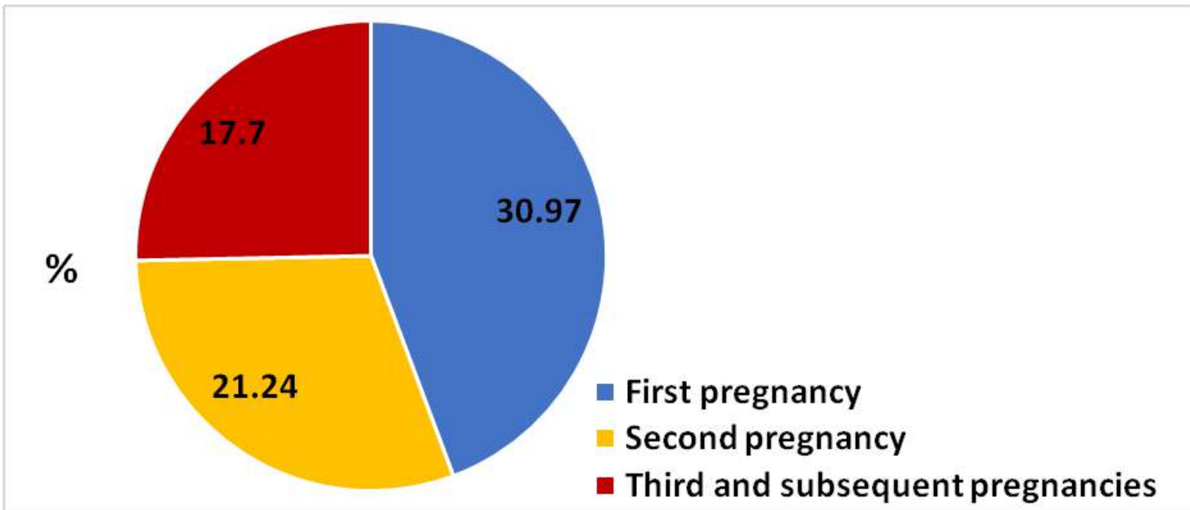


Fig. 3.6. Analysis of the ordinal number of pregnancies from which the child was born

Thus, the proportion of patients born as a result of the first and second pregnancies prevails, which may have potential significance for further analysis of risk factors for the development of anemic conditions in children.

Analysis of the distribution of children by type of feeding showed a relatively low level of prolonged breastfeeding in the studied cohort, which could potentially be a risk factor for the development of anemia at an early age (Fig. 3.7). In particular, only 15 children were exclusively breastfed up to 6 months, which corresponds to current WHO recommendations, while 12 babies were breastfed up to one year. In another 10 children, the duration of breastfeeding exceeded one year, which can be considered a positive factor in the formation of hematological status. At the same time, artificial feeding was recorded in 10 patients, which may be associated with higher risks of developing iron deficiency anemia, given the lower bioavailability of iron in adapted mixtures compared to breast milk. Mixed feeding was rare - only in one patient.

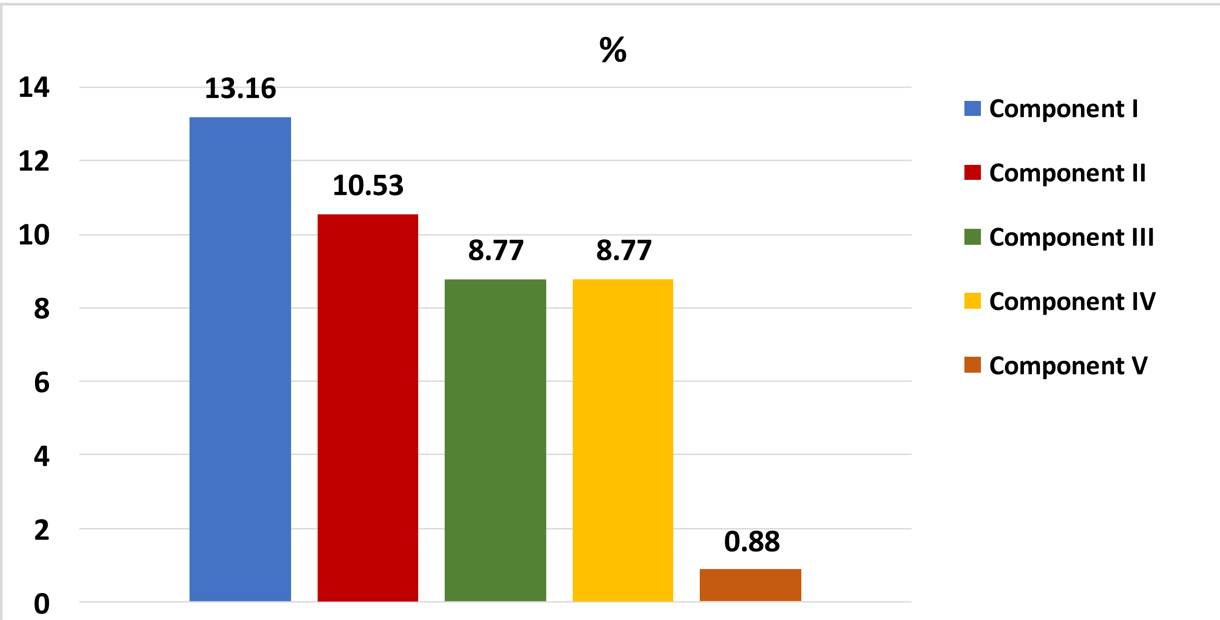


Fig. 3.7. Analysis of the type of infant feeding

Note: Legend: 1 – Breast feeding up to 6 months; 2 – Breast feeding up to 1 year; 3 – Breastfeeding beyond 1 year; 4 – Formula feeding; 5 – Mixed feeding

Overall, the analysis of feeding patterns suggests a significant diversity of feeding strategies in early childhood among children hospitalized with anemia. Insufficient breastfeeding coverage in the first six months of life, as well as low duration of breastfeeding, may be important factors that require further investigation in the context of prevention of deficiency states, particularly among at-risk groups.

Thus, in the study of clinical and epidemiological features of children with anemia, it was found that the average age of patients reaches 9,07 ± 1,88 years with a predominance of older age groups (14–18 and 6–11 years), which may indicate an increased frequency of anemia in adolescence. Analysis of socio-economic status revealed a significant number of families with signs of social disadvantage, which probably affects the timeliness of diagnosis and accessibility of medical care. In most cases, the family history was unencumbered (73,5%), but 26,5% indicated a possible genetic predisposition to the disease. The obstetric history was normal in almost all cases, and children were born mainly from the first or second pregnancies. The low level of prolonged breastfeeding in the first 6 months of life was also highlighted as a potential risk factor for deficiency states.

In general, the obtained data allow us to outline a specific epidemiological portrait of children with anemia, which is the basis for further division of the studied cohort into groups.

3.2. Clinical, epidemiological and anamnestic characteristics of children with anemia

The average duration of inpatient treatment was 14,7 ± 0,97 bed days. The length of stay of children in the hematology department ranged from several days to more than three weeks (Fig. 3.8).

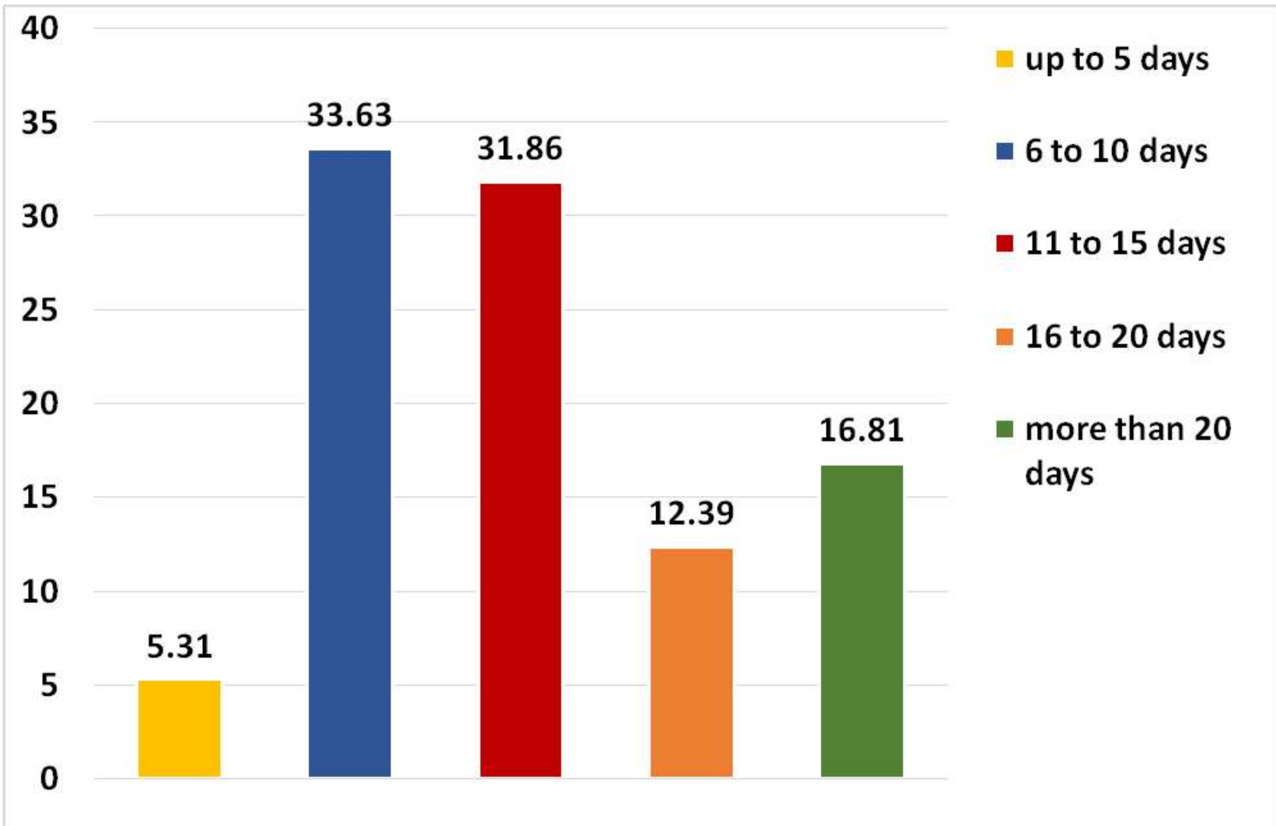


Fig. 3.8. Distribution according to the length of hospital stay in the hematology unit

Thus, the vast majority of patients (over 65%) were hospitalized for 6–15 days. The most common were hospitalizations lasting 6–10 days and 11–15 days, which indicates a medium-long period of hospitalization for most patients. Long-term hospitalizations (over 20 days), recorded in 16,81% of children, may be associated with severe forms of chronic anemia, comorbidities, or the need for a comprehensive therapeutic approach.

Analysis of the duration of the disease among children hospitalized with anemia showed that in 51 children anemia was detected for the first time during this visit (Fig. 3.9).

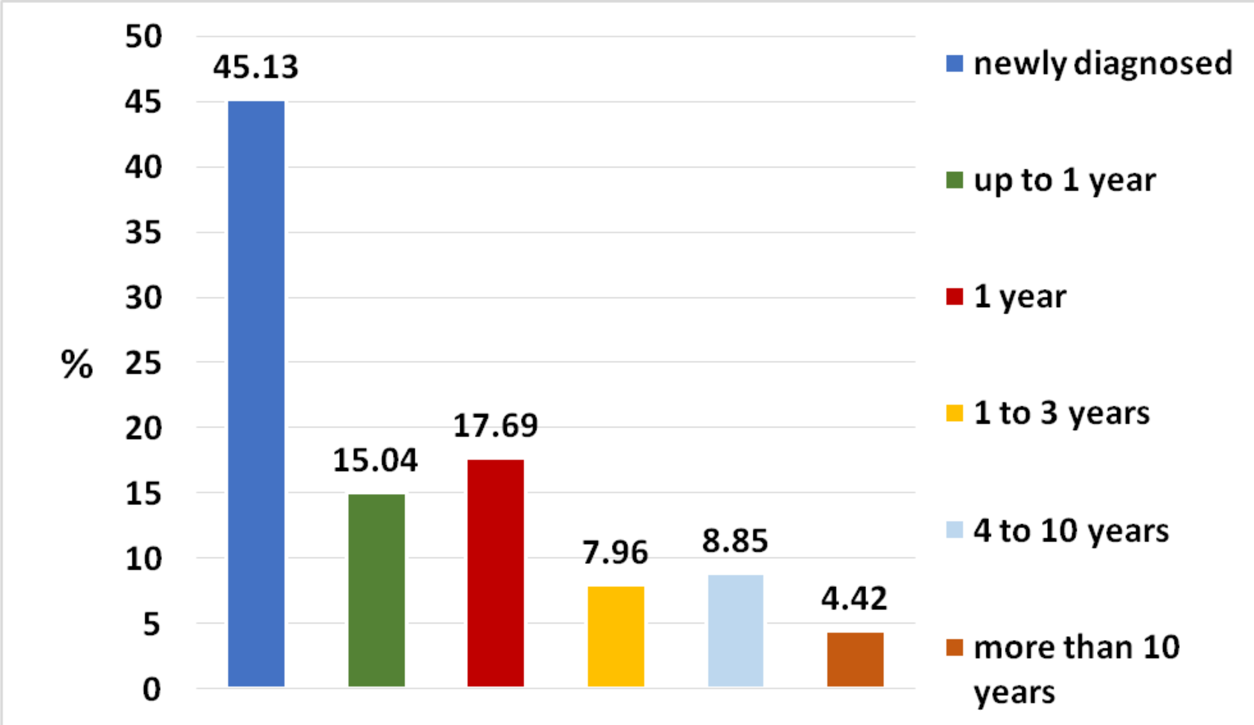


Fig. 3.9. Distribution according to the length of illness

Thus, almost half of the cases were initially diagnosed, while in the remaining patients anemia had a chronic course of varying duration. Chronic forms of anemia (lasting more than 1 year) were observed in 38,92% of children, which emphasizes the importance of long-term monitoring and preventive measures to prevent disease progression.

Analysis of clinical diagnoses in the sample of hospitalized children showed a significant diversity of forms of anemia, distributed into eight categories (Fig. 3.10). The largest proportion was accounted for by cases of iron deficiency anemia — 72 patients, however, polydeficiency anemia was recorded in 16 children, and congenital hemolytic anemia, represented by hereditary spherocytosis, — in 15 patients. Aplastic anemia was less common: the congenital form — in 2 children, and the acquired — in 4 patients. 2 cases of chronic posthemorrhagic anemia were also recorded. Congenital nonspherocytic hemolytic anemia was diagnosed in two patients.

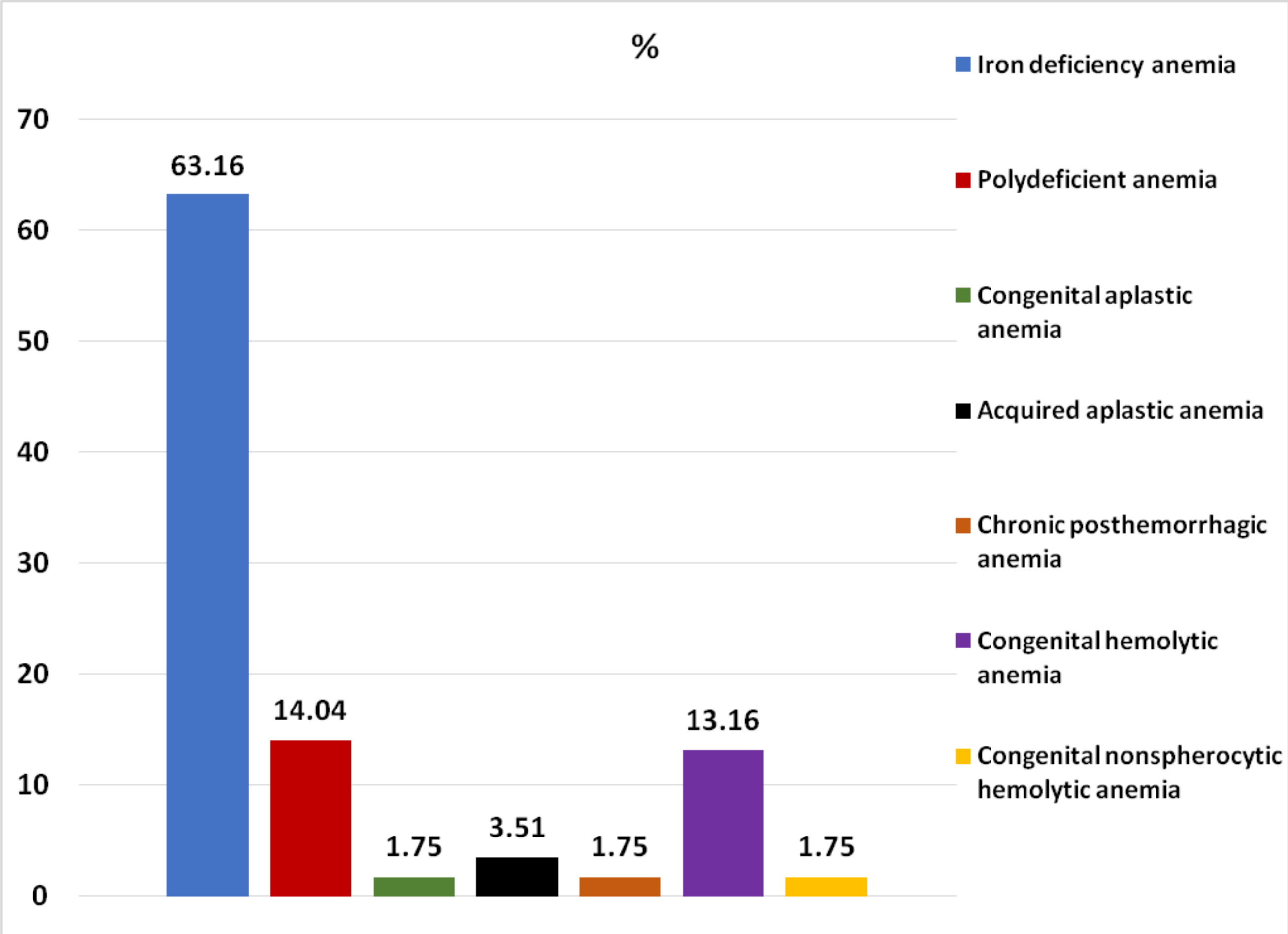


Fig. 3.10. Analysis of the structure of clinical diagnoses

The results obtained indicate the dominance of iron deficiency states among children with anemia, while at the same time indicating the presence of rarer, but clinically significant forms of pathology.

The total sample of children studied consists of two main groups, differing in the type of anemia: congenital and acquired (Fig. 3.11).

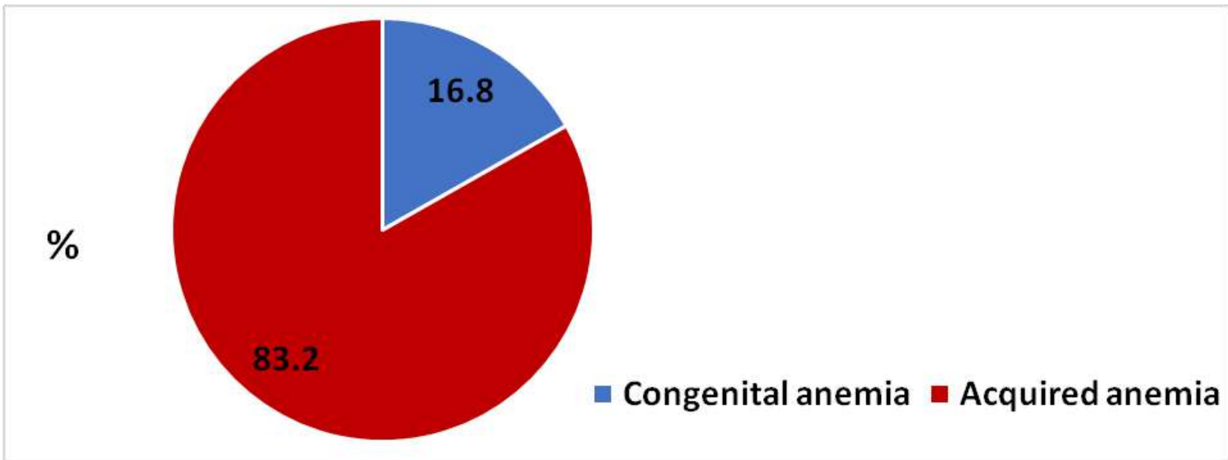


Fig. 3.11. Analysis of the (%) registration of anemia types (congenital/acquired) in children

A group of 19 children with congenital anemias, among which such subtypes as congenital hemolytic anemia, including hereditary spherocytosis, aplastic anemias, and non-spherocytic hemolytic anemia, were identified. The second group consists of 94 children with acquired forms of anemia, which arose as a result of various environmental factors or internal disorders of the body, which led to the development of this disease.

Analysis of the presence of complications in hospitalized children with anemia showed that in the vast majority of patients — 110 children — the course of the disease was not accompanied by complications (Fig. 3.12). Complicated course of anemia was recorded in only 3 people. The data obtained indicate that most cases of anemia in the studied sample were characterized by a relatively favorable clinical course without severe consequences or concomitant pathological conditions.

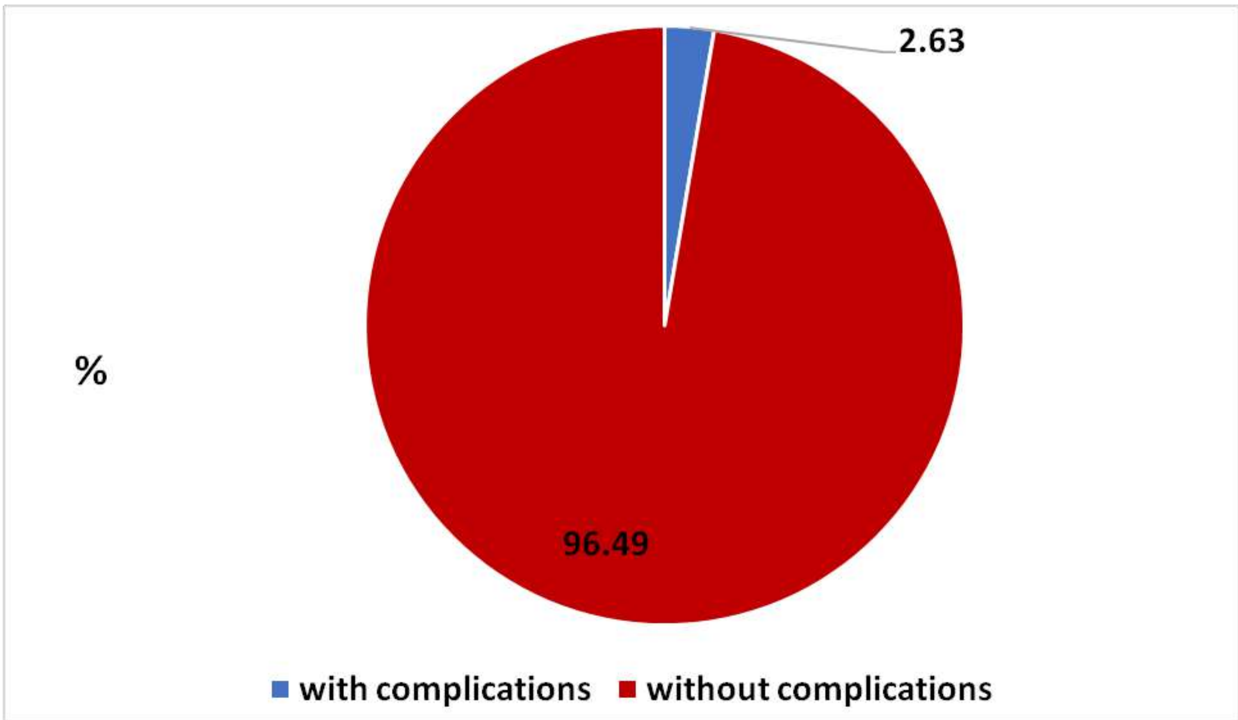


Fig. 3.12. Analysis of the hospitalization period in children

The data obtained indicate that most cases of anemia in the studied sample were characterized by a relatively favorable clinical course without severe consequences or concomitant pathological conditions.

Analysis of the distribution of patients by the primary diagnosis of anemia demonstrated an almost complete balance between cases of newly detected anemia and previously diagnosed disease. In particular, in 50% of children anemia was diagnosed for the first time in a hospital, while the other 50% of patients were admitted to the hospital with a previous diagnosis, which indicates a continuation or relapse of an already known pathological process. Such a uniform distribution is indicative and has several clinically important aspects. On the one hand, a significant proportion of primary cases may indicate an insufficient level of primary medical diagnosis and the absence of effective mechanisms for early detection of anemia in the pediatric population. On the other hand, almost the same number of repeated diagnoses indicates a tendency of some patients to chronicity of the pathological process or to the presence of forms of anemia that require long-term observation, correction and periodic hospitalizations.

Analysis of the distribution of hospitalized children by the presence of concomitant diagnoses (Fig. 3.13) showed that the vast majority of patients — 90 people — did not have concomitant diseases. This may indicate an isolated course of anemia in most cases, which simplifies the diagnostic search and allows you to focus treatment measures without the need to take into account additional somatic or chronic conditions. In 23 children, the presence of concomitant pathology was detected, which requires special attention from clinicians, since comorbid conditions can affect both the pathogenesis of the underlying disease and the effectiveness of therapeutic interventions.

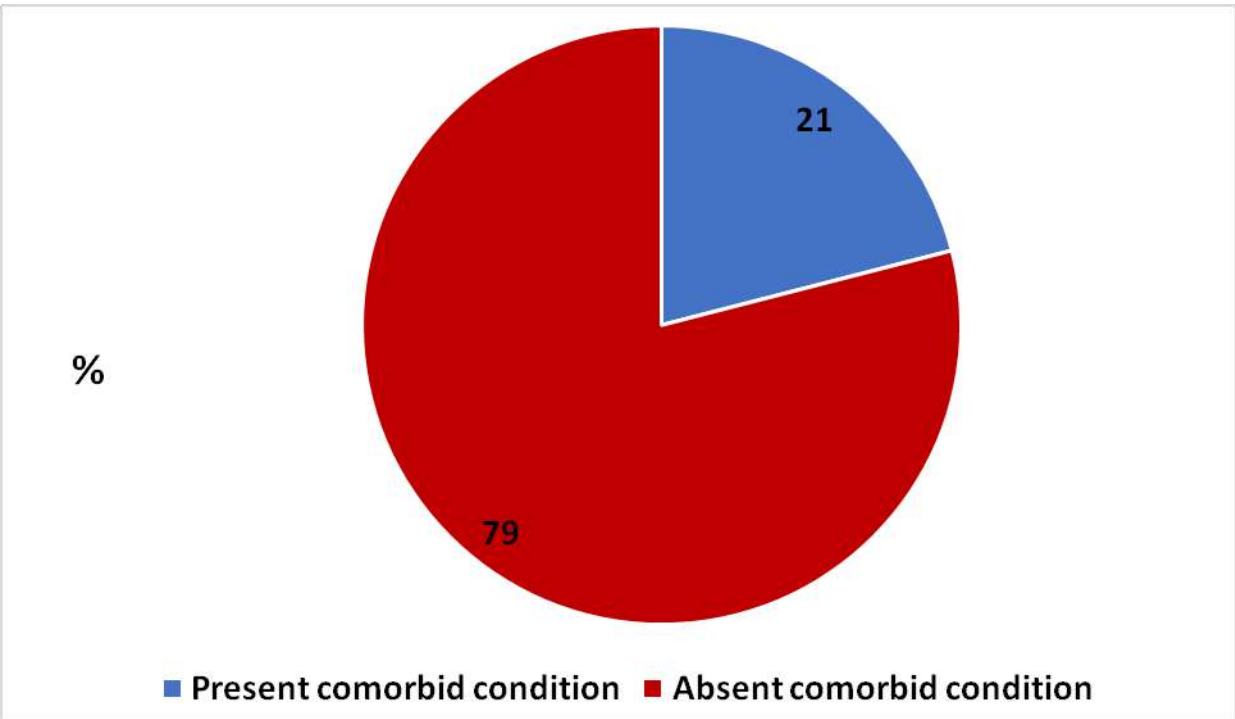


Fig. 3.13. Analysis of the presence of comorbid diagnoses

Thus, despite the dominance of isolated forms of anemia, the presence of concomitant diseases in every fifth patient justifies the need for an interdisciplinary approach to the diagnosis and treatment of such children.

A comprehensive analysis of anamnestic data on past and concomitant diseases in children with anemia revealed a predominantly isolated nature of the pathology in most cases (Fig. 3.14). In particular, 108 children did not have any significant past diseases in their history, which indicates a generally satisfactory somatic status of the patients before hospitalization. Only 5 children had a history of frequent acute respiratory viral infections.

Regarding comorbidity (Fig. 3.14), 93 children had no registered comorbidities, which further emphasizes the presence of anemia as the main clinical diagnosis without a pronounced comorbid background. However, 20 children still had comorbidity, which may indicate potential factors that probably complicate the course of anemia and require separate analysis.

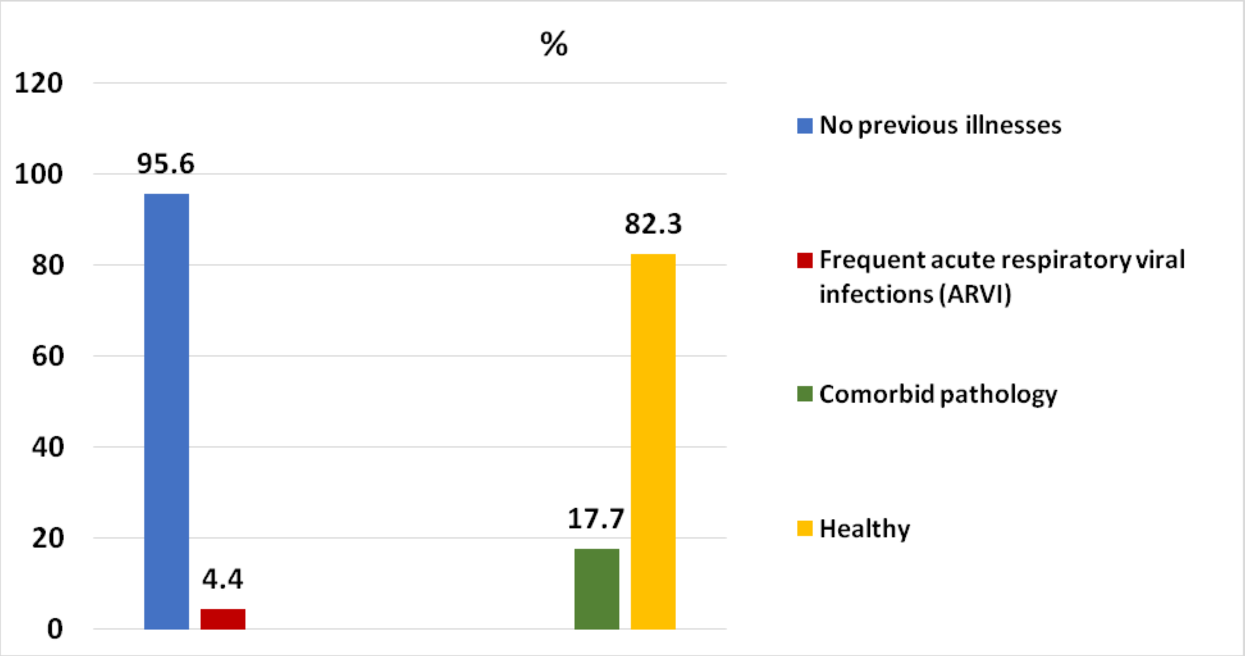


Fig. 3.14. Analysis of the somatic status and comorbid pathology in children

Note: Legend – 1: Somatic status, 2: Comorbid pathology.

Thus, the analysis of clinical data of children hospitalized with anemia to the hematology department of the CRCH showed that the average duration of inpatient treatment was 14,7 ± 0,97 bed days, and the vast majority of cases were characterized by a medium-long stay (6–15 days). At the same time, in more than a third of children, bullous anemia was detected for the first time during the current hospitalization, while in the remaining analyzed cases the disease was chronic, which necessitates long-term monitoring. The largest share of clinical diagnoses was iron deficiency anemia, which coincides with the literature data [8, 9] and indicates their dominance among pediatric hematological pathologies. In most cases, anemias occurred without complications (97,3%) and without concomitant diagnoses (over 80%), which determines their relatively isolated and favorable clinical course. At the same time, the presence of concomitant pathologies in every fifth patient emphasizes the need for an interdisciplinary approach to the management of such patients.

The obtained data generally reflect the clinical portrait of a hospitalized pediatric sample with anemia, emphasizing the prevalence of iron deficiency conditions, moderate duration of hospitalization, and a predominantly favorable course of the disease without significant malnutrition.

CHAPTER 4
FEATURES OF THE COURSE OF ANAEMIA IN CHILDHOOD PATIENTS BEFORE THE BEGINNING AND DURING THE WAR IN UKRAINE

4.1. Clinical and epidemiological profile of children with anemia in comparison groups

A comparative analysis of the demographic characteristics of children with anemia of groups I and II revealed a number of important differences that deserve attention in the context of an epidemiological assessment of the impact of the war on the condition of the child population.

Gender distributiondemonstrates a tendency towards a predominance of girls in group I (58,2%) versus 47,8% in group II and, accordingly, a smaller proportion of boys 41,8% in group I versus 52,2% in group II ($P\varphi>0,05$). Despite the apparent difference, no statistically significant differences were recorded, which indicates a generally comparable gender structure in the samples.

The age of children at the time of hospitalization did not differ between groups: in clinical group I the average age was 9,2±5,53 years, in children hospitalized with anemia in the pre-war period – 9,9±5,76 years ($P>0,05$).

Place of residencealso shows a non-significant difference. The proportion of children living in urban conditions was lower in group I (32,8%) compared to group II (45,7%), while rural residents prevailed in group I (67,2% versus 54,3% in group II ($P\varphi>0,05$)). Although the level of statistical significance was not reached, this trend may indicate an increase in the vulnerability of rural children in conditions of military instability.

In general, the results of demographic data of patients in group I versus those in group II indicate that children who came under observation after the start of hostilities in Ukraine more often lived in rural areas and were characterized by a slight predominance of females.

A comparison of the distribution of blood groups among children with anemia belonging to groups I (during the war) and II (pre-war period) revealed some differences in the frequency of individual phenotypes.

The most common among the comparison children, blood group A (II) was the same as in the general population. Despite the relative predominance of this group in the cohort after the start of the war, the difference did not reach statistical significance (Fig. 4.1).

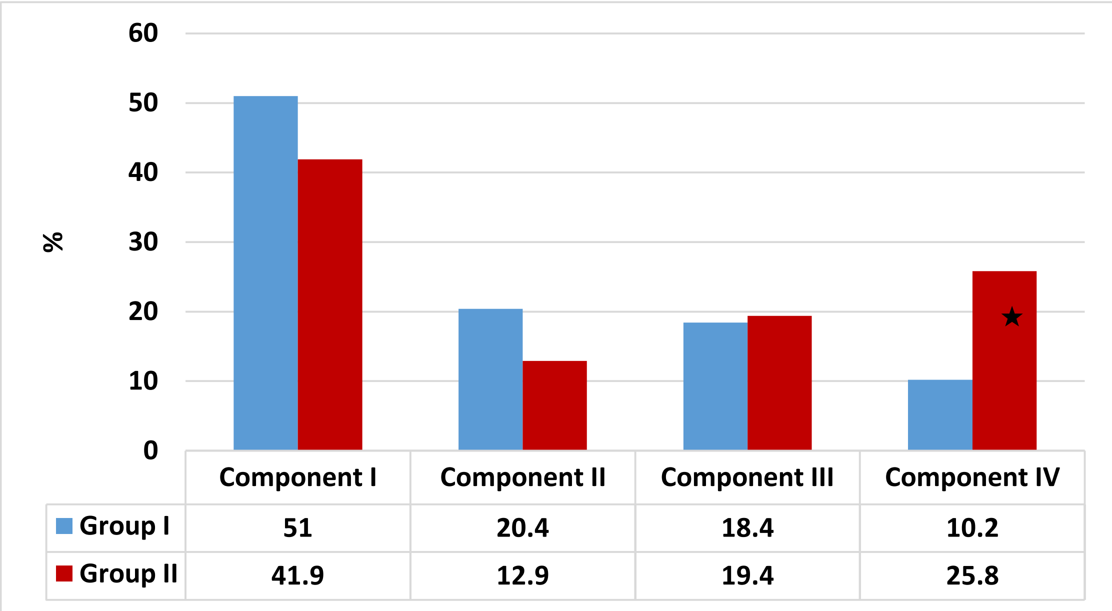


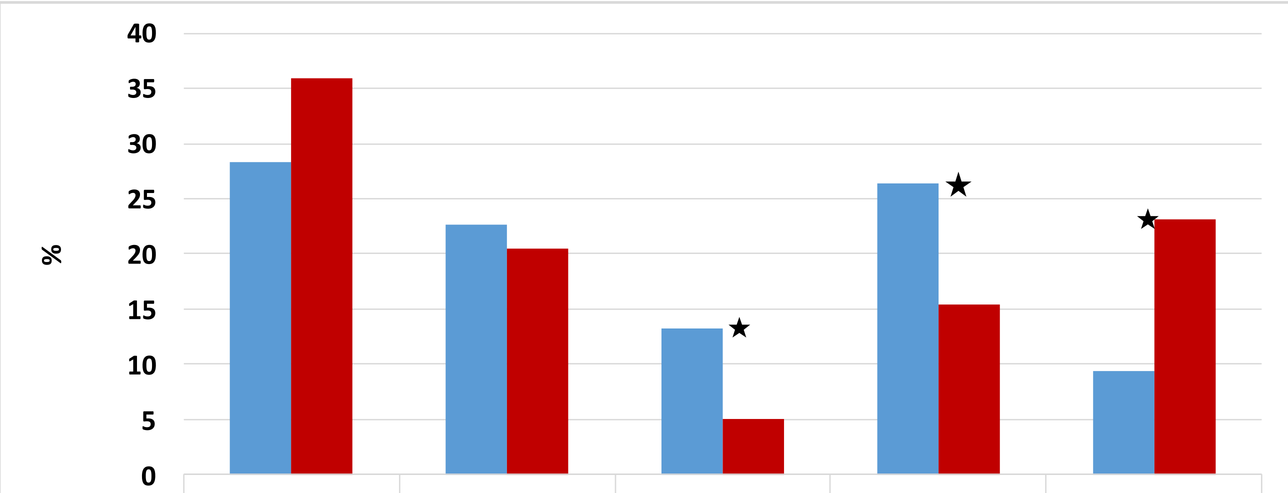
Fig. 4.1. Frequency (%) of blood groups in hospitalized children

Note: Legend: I – blood group 0, II – blood group A, III – blood group B, IV – blood group AB.

★- (Pφ<0,05)

So, blood type 0 (I) was observed in children of group I with a slight predominance over the number of patients in group II. Blood group B (III) was almost equally distributed in both groups, indicating the complete absence of significant differences. The most noticeable difference was observed in the frequency of blood group AB (IV). Thus, the results obtained indicate a potential decrease in the frequency of the rare blood group AB in the post-war cohort of children with anemia.

Analysis of the age characteristics of patients with newly diagnosed anemia allowed us to establish differences between clinical groups I and II. The first group was dominated by children in whom anemia was diagnosed at the age of 6 to 11 years and in adolescence (11 to 14 years). A significantly lower percentage was made up of adolescents aged 14 to 18 years. In contrast, in the second group, the largest number of cases of primary diagnosis of anemia was in the age group up to 3 years and from 14 to 18 years, and the smallest number was in children aged 6 to 11 years (Fig. 4.2).



	I Component	II Component	III Component	IV Component	V Component
Group I	28.3	22.6	13.2	26.4	9.4
Group II	35.9	20.5	5.1	15.4	23.1

Fig. 4.2. Frequency (%) of age groups at initial diagnosis of anemia in children

Note: Legend:I - under 3 years of age, II - 3.1 years - 6 years, III - 6.1 years - 11 years, IV - 11.1 years - 14 years, V - 14.1 years - 18 years

★- (Pφ<0,05)

Thus, in clinical group I, an earlier detection of anemia was observed in middle and senior school age, which may indicate differences in the characteristics of the course of the disease or the level of parental alertness. In turn, in clinical group II, a higher proportion of cases of anemia detection in senior school age may indicate a later manifestation of symptoms or a delay in diagnosis. These age-related features deserve further study in the context of the earliest diagnosis of anemia in pediatric patients.

According to the results obtained, it can be concluded that the cohort of children of secondary school age from 11 to 14 years old is the most vulnerable in the circumstances that have developed in Ukraine today (active hostilities), since it is in this age group that the incidence of anemia is probably higher compared to schoolchildren in peacetime. This assumption is also confirmed by the clinical and epidemiological indicators obtained by us. Thus, the relative risk of developing iron deficiency anemia in children during active military operations compared to peacetime increases almost 2 times, and the odds ratio is almost 3, AR – 24,3%, RR – 1,5 (95% CI: 0,6-4,0), OR – 2,8 (95% CI: 0,9-8,2).

At the same time, the analysis of the time of the last episode of the disease in both groups allows us to identify the features of the course of anemia, taking into account its chronological development. In the first group, which is represented mainly by primary referrals, the largest proportion is made up of cases where anemia was diagnosed for the first time — 35 children. A somewhat smaller proportion of anemia was registered more than 6 months ago — 15 children, as well as 3–6 months before hospitalization — 11 children. Only 6 patients became ill during the last month. In the second group, which includes mainly repeated referrals, the proportion of children with a long history of the disease (more than 6 months) is the largest — 22 children, which indicates the chronic nature of its course. First-detected anemia in this group was observed in 13 children, which is a significantly lower rate than in group I. Other intervals — up to 1 month and 3–6 months — were observed in 2 and 9 children, respectively (Fig. 4.3).

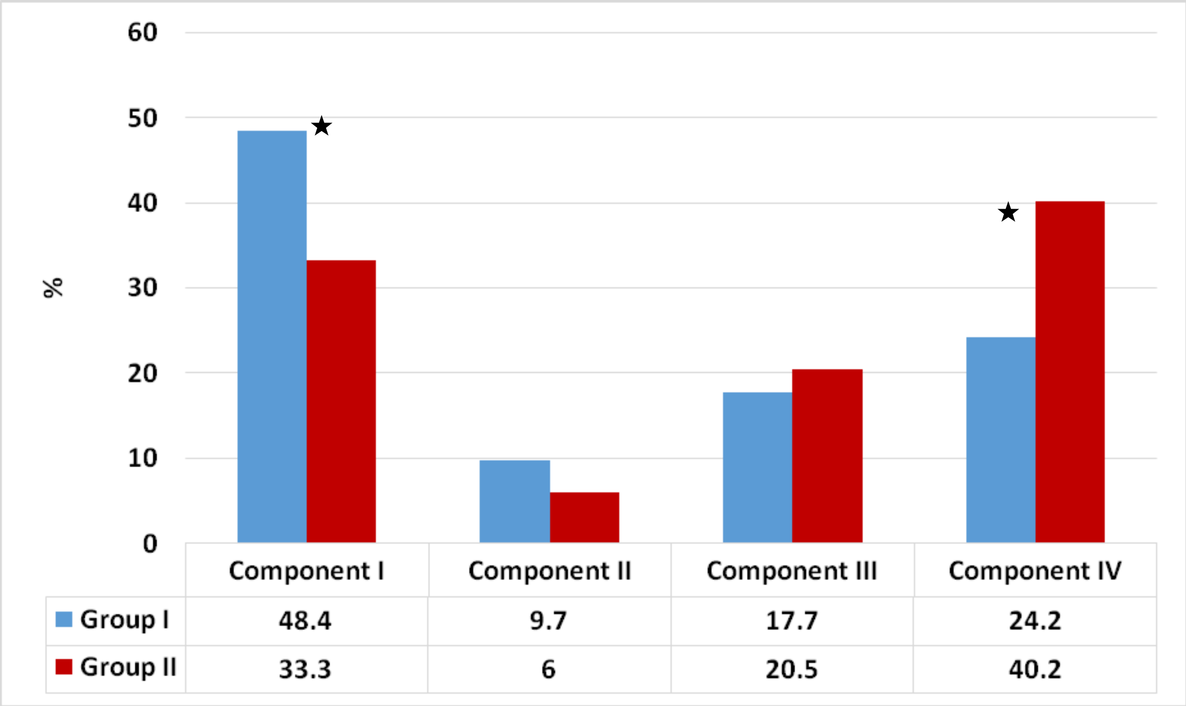


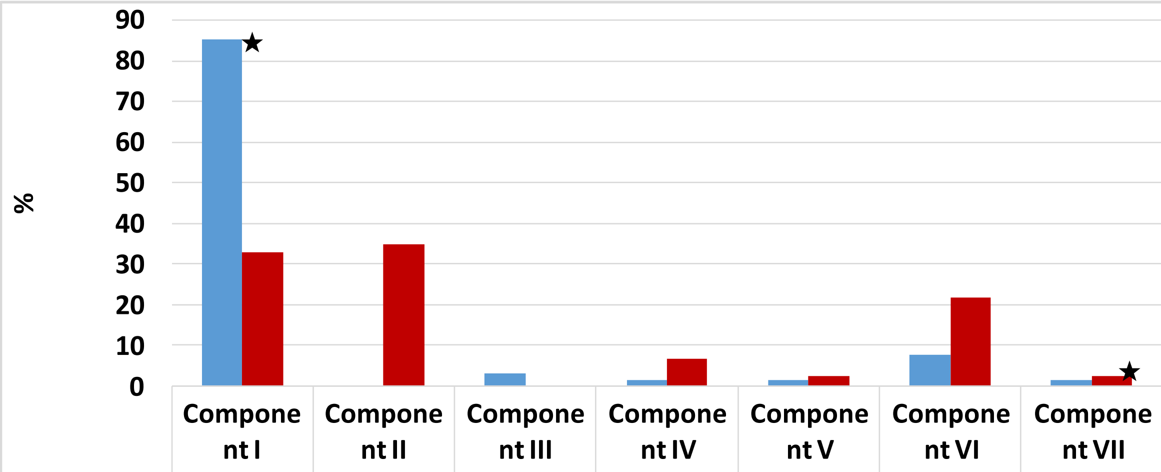
Fig. 4.3. Frequency (%) of the most recent manifestations of anemia in the comparison groups

Note: Legend:I – newly diagnosed anemia; II – less than 1 month; III – 3 to 6 months; IV – more than 6 months

★- (Pφ<0,05)

Comparison of both groups by different categories of episode time reveals significant differences, indicating a statistically significant predominance of such cases in group I. In contrast, the categories associated with a more recent onset of the disease — “3–6 months ago” and “more than 6 months ago” confirm a statistically higher proportion of chronic forms of the disease in group II. The category “up to 1 month” has a moderate positive difference, although its total share in the sample is small. Our results indicate differences in the clinical course of anemia between the groups: in group I, cases of the disease diagnosed for the first time dominate, while in group II there is a tendency towards a long, recurrent or chronic course.

Analysis of clinical diagnoses in the two studied groups of hospitalized children revealed a significant diversity of forms of anemia, distributed into seven categories (Fig. 4.4).



	Component I	Component II	Component III	Component IV	Component V	Component VI	Component VII
Group I	85	0	2.9	1.4	1.4	7.4	1.4
Group II	32.6	34.7	0	6.6	2.2	21.7	2.2

Fig. 4.4. Frequency (%) of recorded diagnoses in children from the comparison groups

Note: Legend: I - Iron deficiency anemia, II - Polydeficient anemia, III - Congenital aplastic anemia, IV - Acquired aplastic anemia, V- Chronic posthemorrhagic anemia, VI - Congenital hemolytic anemia, VII - Congenital nonspherocytic hemolytic anemia

★- (Pφ<0,05)

It should be noted that the largest proportion of cases was iron deficiency anemia - 57 patients in group I versus 15 patients in group II, which coincides with the data literature [72-75] and indicates their clinical superiority among hematological pathologies. In contrast, polydeficiency anemia was found only in 16 children of the second group, and congenital aplastic anemia was found only in 2 children of the first group. Congenital hemolytic anemia, represented by hereditary spherocytosis, was found in 5 patients of the first group versus 10 patients of the second group. Aplastic anemia was found much less frequently: the first group - in 1 patient, the second group - in 3 examined. Also, 1 case of chronic posthemorrhagic anemia was recorded in patients from both groups.

Thus, the analysis of clinical diagnoses revealed significant variability in the forms of anemia among hospitalized children, with a predominance of iron deficiency anemia, which was statistically more common in group I. It should be noted that the predominant proportion of congenital anemias (58,6%) is represented in the group of patients who were treated in the pre-war period. The results obtained reflect both the clinical dominance of iron deficiency conditions and the need for a differentiated approach to the diagnosis and treatment of various forms of anemia in children, depending on the etiology and context of hospitalization.

At the same time, the relative risk of developing iron deficiency anemia in children during active military operations increases almost 4 times compared to peacetime, and the odds ratio is almost 12, AR – 50,0%, RR – 3,9 (95% CI: 2,9-5,3), OR – 11,7 (95% CI: 5,8-23,4).

Analysis of previous treatment of children with anemia in both groups indicates significant differences in the tactics of patient management at the time of inclusion in the study. Thus, in group I, more than half of the children — 35 patients — did not receive any treatment at the prehospital stage, which indicates a significant proportion of undiagnosed or ignored cases of anemia in the population. However, specific therapy aimed at correcting the anemic state was received by 27 children, which demonstrates the presence of a certain level of awareness among parents about the need for targeted treatment. Symptomatic treatment, without an etiotropic approach, was received by only 5 children.

In contrast, a slightly different distribution is observed in group II: 18 children had no treatment experience, which is a lower figure compared to group I, while 17 children received specific therapy, and the proportion of symptomatic treatment increased to 11 children. This may indicate that some children in group II are under observation with chronic anemia, but the treatment is not always targeted (Fig. 4.5).

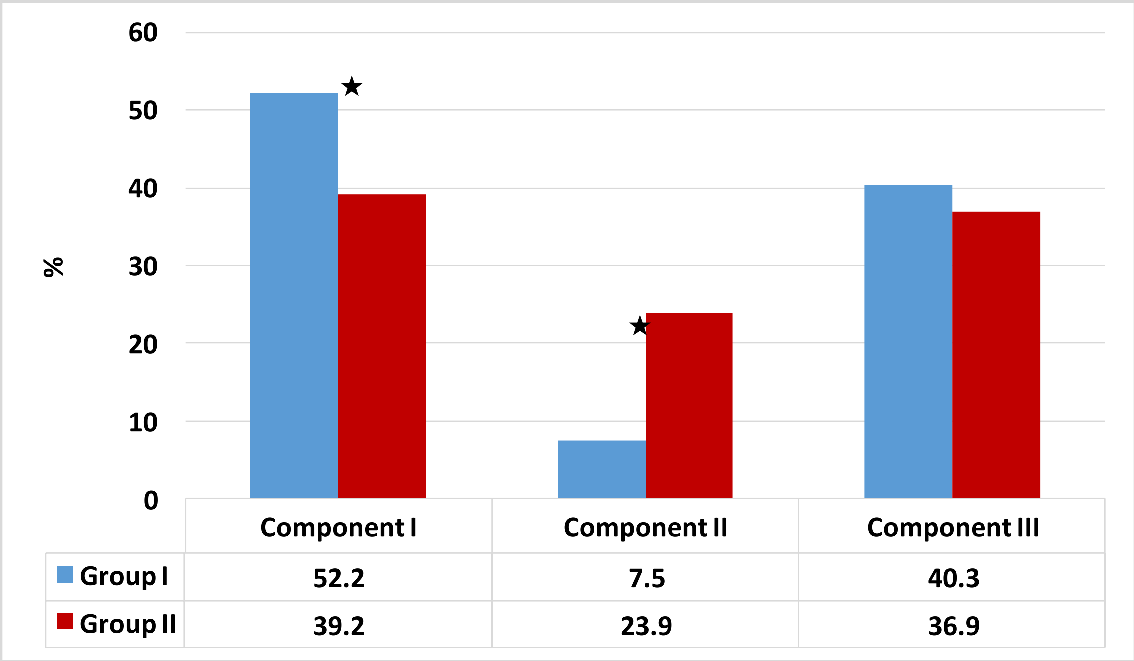


Fig. 4.5. Distribution (%) of treatment modalities across the comparison groups

Note: Legend: I – no treatment received, II – symptomatic therapy, III – specific therapy.

★- (Pφ<0,05)

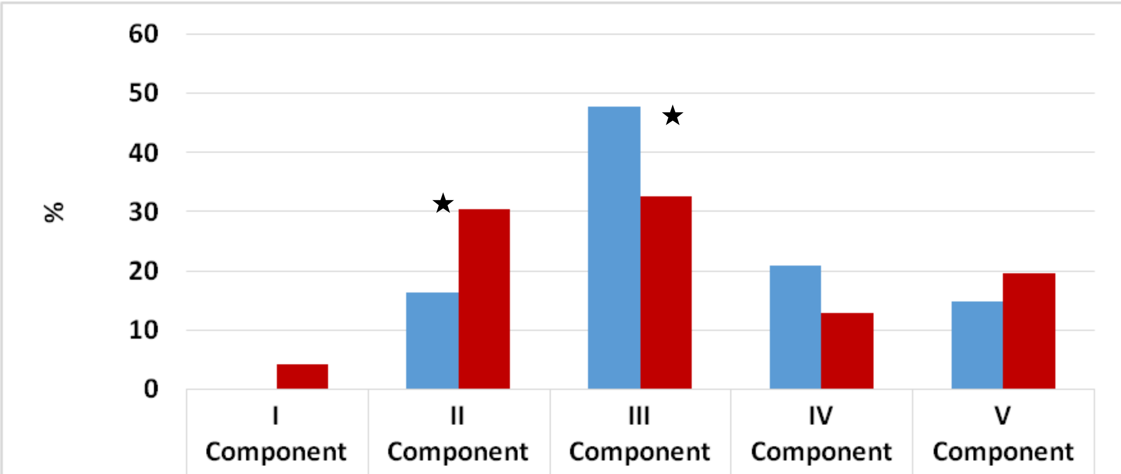
Comparative analysis between groups shows the greatest difference in the category of symptomatic treatment, indicating a significantly higher proportion of such cases in group II. However, the category "did not receive treatment before hospitalization" prevails in group I. The difference is less pronounced in the category "specific therapy at the prehospital stage", indicating a relatively uniform use of targeted treatment in both groups.

So, in the group of patients who were hospitalized in the CRCH since the beginning of the war in Ukraine, the majority were girls - residents of the village with blood group 0 (I), in whom the vast majority had first-time iron deficiency anemia.

In contrast, among patients who underwent inpatient treatment for anemia in the pre-war years, boys, urban residents with blood group IV, with repeated cases of questioning mainly for multiple deficiency anemia, predominated.

4.2. Clinical features of the course of anemia in children in peacetime and wartime

Pale skin is one of the most common clinical signs of anemia. Thus, in our study, the results of group I demonstrate a higher frequency of severe manifestations of pale skin, while in group II milder forms or complete absence of the symptom were more often recorded (Fig. 4.6).



	I Component	II Component	III Component	IV Component	V Component
Group I	0	16.4	47.8	20.9	14.9
Group II	4.3	30.4	32.6	13	19.6

Fig. 4.6. Frequency (%) of recorded skin pallor in children

Note: Legend: I - Absence of the symptom, II - Mild manifestation, III - Moderate manifestation, IV - Marked manifestation, V - Severe manifestation

★- ($P\varphi<0,05$)

A similar trend was observed for mucous membrane pallor, with significantly more pronounced symptoms being recorded less frequently in group I, and slightly more frequently in group II, which may indicate a later period of anemia detection in group II. At the same time, the absence of this symptom was characteristic only for group II (Fig. 4.7).

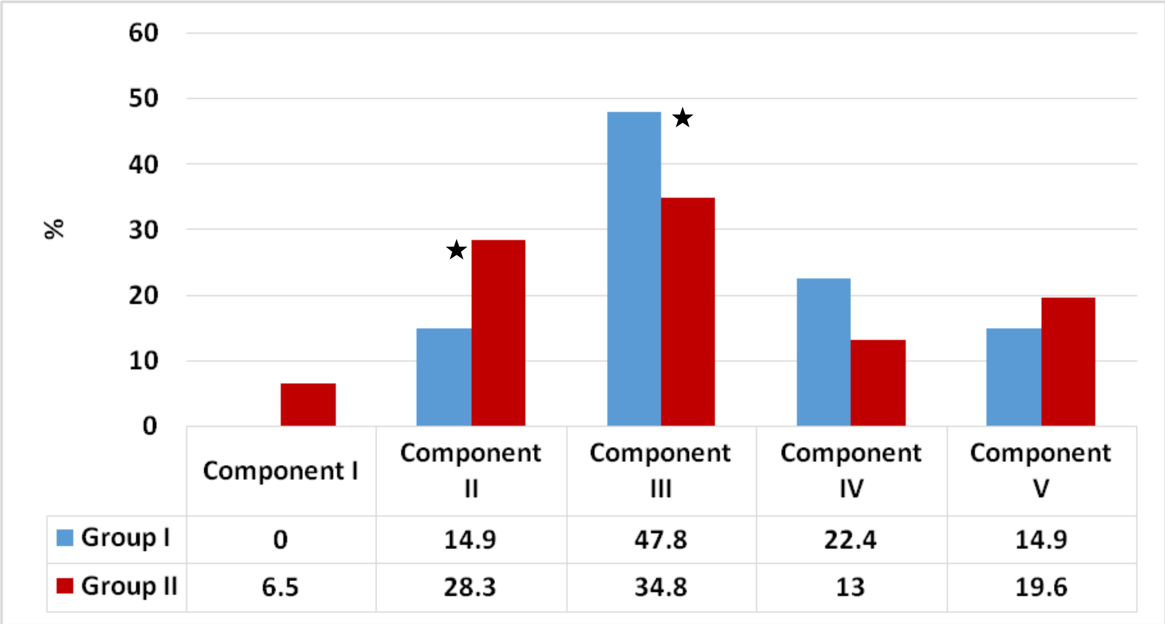


Fig. 4.7. Frequency (%) of recorded mucosal pallor in children

Note: Legend: I – Absence of the symptom, II - Mild manifestation, III – Moderate manifestation, IV – Marked manifestation, V - Severe manifestation

★- ($P\varphi<0{,}05$)

At the same time, the frequency of significantly pronounced manifestations of nail bed pallor remained constant in both groups, however, in group I, the complete absence of the symptom was not recorded, but the number of such cases was somewhat higher, which indicates a potentially milder course of anemia in some children in group II (Fig. 4.8).

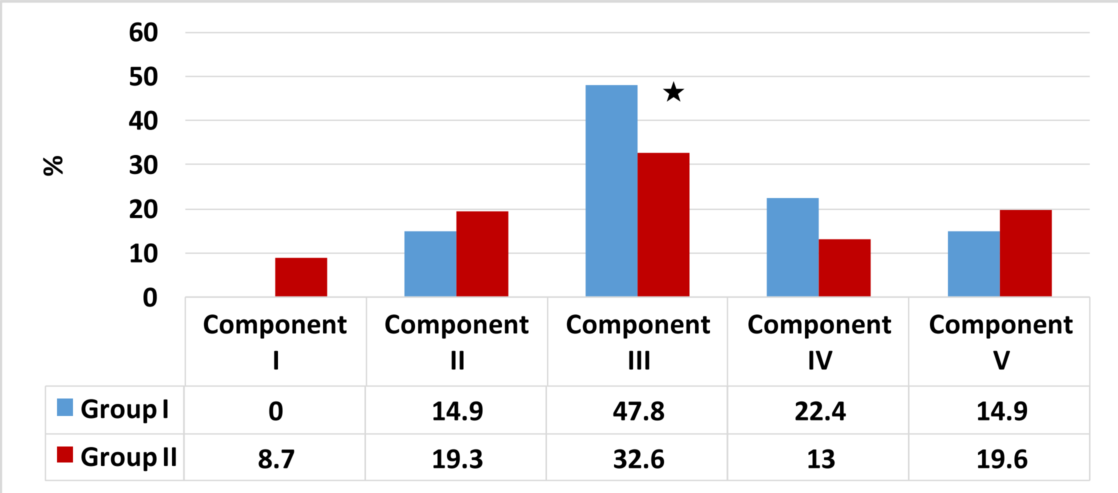


Fig. 4.8. Frequency (%) of recorded nail bed pallor in children

Note: Legend: I – Absence of the symptom, II - Mild manifestation, III – Moderate manifestation, IV – Marked manifestation, V - Severe manifestation

★- ($P\varphi<0,05$)

At the same time, the symptom of a pronounced decrease in appetite was somewhat more common in group I, while moderate manifestations were more common in group II (Fig. 4.9).

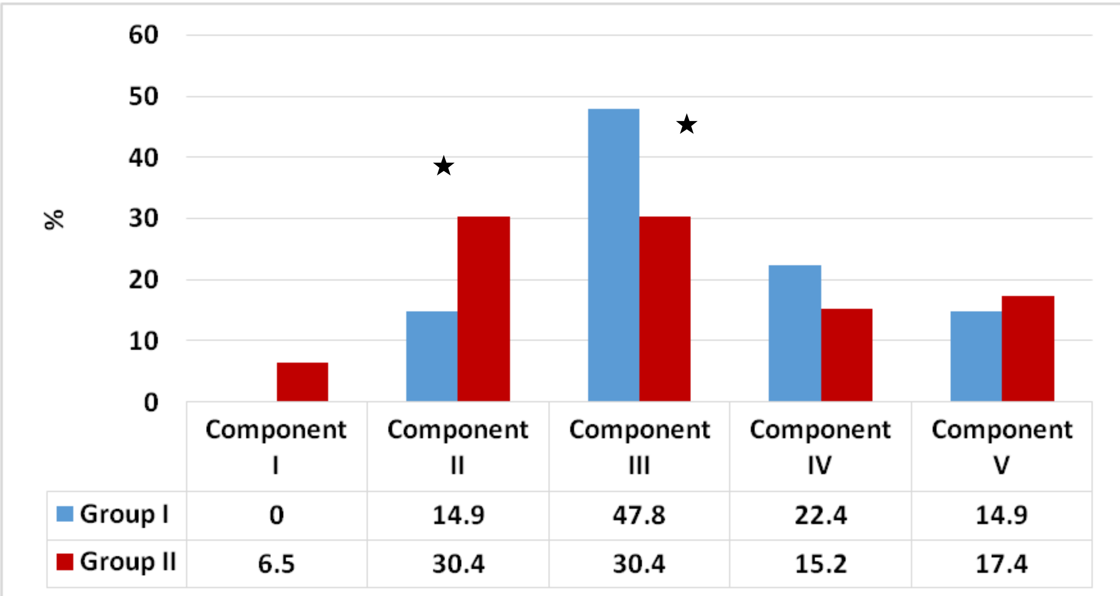
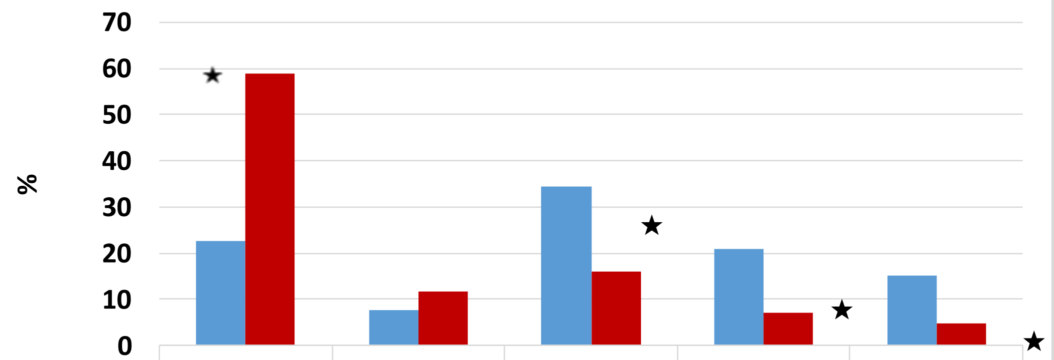


Fig. 4.9. Frequency (%) of recorded decreased appetite in children

Note: Legend: I – Absence of the symptom, II - Mild manifestation, III – Moderate manifestation, IV – Marked manifestation, V - Severe manifestation

★- (Pφ<0,05)

The most striking difference was recorded regarding the consumption of unusual foods: unlike the first clinical group, where a significant proportion of patients had various manifestations of this symptom, in group II more than half of the children had no changes in eating behavior at all, and significantly pronounced changes were observed in only less than 5% of children (Fig. 4.10).



	Component I	Component II	Component III	Component IV	Component V
Group I	22.4	7.5	34.3	20.6	14.9
Group II	58.7	11.4	15.9	6.8	4.5

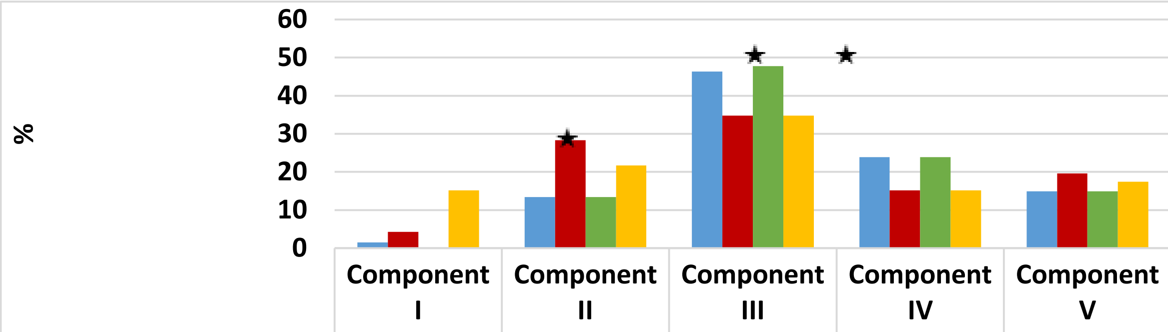
Fig. 4.10. Frequency (%) of consumption of non-nutritive substances in children

Note: Legend: I – Absence of the symptom, II - Mild manifestation, III – Moderate manifestation, IV – Marked manifestation, V - Severe manifestation

★- (Pφ<0,05)

At the same time, the relative risk of developing such a rather specific symptom as eating unusual food in children with anemia during active military operations increases almost twice as much as in peacetime, and the odds ratio is almost 3, AR – 30,0%, RR – 1,6 (95% CI: 0,9-2,6), OR – 2,7 (95% CI: 1,4-5,4).

Drowsiness and fatigue were also somewhat more pronounced in group I. Thus, manifestations of fatigue in a pronounced or significantly pronounced form were observed somewhat more often in children of group I, although the number of individuals with a similar symptom in group II reached almost the same values (Fig. 4.11).



	Component I	Component II	Component III	Component IV	Component V
Group I (fatigability)	1.5	13.4	46.3	23.9	14.9
Group II (fatigability)	4.3	28.3	34.8	15.2	19.6
Group I (drowsiness)	0	13.4	47.8	23.9	14.9
Group II (drowsiness)	15.2	21.7	34.8	15.2	17.4

Fig. 4.11. Frequency (%) of recorded fatigability and drowsiness in children

Note: Legend: I – Absence of the symptom, II - Mild manifestation, III – Moderate manifestation, IV – Marked manifestation, V - Severe manifestation

★- (Pφ<0,05)

Analyzing the severity of anemia in children of the comparison groups, we found that in patients who were hospitalized during active military operations, almost every second examined person had severe and moderate forms of the disease (49,9%) and the opposite was true for patients hospitalized in peacetime (34,8%, (Pφ<0,05)).

At the same time, the relative risk of developing severe and moderate forms of anemia in children during active military operations compared to peacetime increases by 2 times, and the odds ratio is almost 2, AR – 15,0%, RR – 1,7 (95% CI: 0,9-1,9), OR – 1,9 (95% CI: 1,1-3,3).

Overall, the results indicate a more pronounced clinical picture of anemia in children admitted after the start of the full-scale war in Ukraine. The data obtained may possibly indicate insufficient access to medical care, diagnostics, or nutrition in war conditions, which requires further analysis.

4.3. Analysis of the results of laboratory and instrumental studies in children of comparison groups of patients with anemia

A comparative analysis of the general clinical blood test upon admission in children with anemia, divided into groups according to the time of hospitalization, presented in Table 4.1, revealed a number of differences that indicate the peculiarities of the course of the disease in modern conditions.

Table 4.1

Study groups	HGB	RBC	Reticulocytes, %	PLT	WBC	**ESR**	LYM, %	Bands ,%	Segs, %	Eosinophils, %	Monocytes, %
Group I	90.8± 3.01	3.9± 0.14	1.3± 0.41	362.1± 19.33	8.6± 0.54	7.6± 0.59	39.3± 1.91	5.2± 0.44	45.8± 1.88	4.5± 1.25	5.6± 0.55
Group II	94.6± 4.36	4.3± 0.13	5.9± 1.01	373± 37.23	9.6± 1.66	10.3± 2.19	31.2± 2.34	4.5± 0.36	59.2± 2.39	2.3± 0.28	3.2± 0.32
P	>0.05	>0.05	<0.05	>0.05	>0.05	<0.05	<0.05	>0.05	>0.05	>0.05	>0.05

Hemoglobin levelin the blood of patients in group I were slightly lower compared to group II, which may indicate a more severe degree of anemic syndrome in children hospitalized after the start of full-scale war. Although the difference is not large, it reflects the general trend towards worsening hematological indicators during the war period.

The slightly lower average value of erythrocytes in the blood of patients in group I than in group II — 4,3×10^{12}/l may indicate a more pronounced suppression of erythropoiesis or a hyporegenerative nature of anemia in group I.

The number of reticulocytes in the blood was significantly lower in patients hospitalized during active military operations compared to children in the second group. This difference may indicate low compensatory bone marrow activity in the first group, which corresponds to the regenerative type of anemia in group II and hyporegenerative in group I.

The average level of platelets in the blood was slightly lower in patients in group I compared to group II, however, both values were within normal limits, which does not indicate clinically significant disorders of thrombocytopoiesis.

In general, the results of group I are characterized by lower erythrocyte and reticulocyte counts, which indicates poorer adaptation of the body to anemia and possible impaired bone marrow function during the war period. While the results of group II demonstrate a higher level of regeneration, which indicates better compensation for the anemic state.

We conducted a repeated comparative analysis of the indicators of the general clinical blood test obtained in the dynamics of treatment of children with anemia, which allows us to assess the effectiveness of therapy and the adaptive reactions of the body in two clinical groups (Tabl. 4.2).

Table 4.2

Study groups	HGB	RBC	Reticulocytes, %	PLT	WBC	**ESR**	LYM, %	Bands ,%	Segs, %	Eosinophils, %	Monocytes, %
Group I	95.9± 2.85	4.5± 0.13	0.7± 0.1	371.9± 29.2	7.6± 0.6	7± 1.96	34.2± 1.97	4.6± 0.34	47.9± 3.02	6.1± 2.65	6.1± 0.6
Group II	102.6 ±3.94	4.5± 0.15	0.9± 0.13	361.7± 35.58	9.5± 1.71	9.7± 3.16	37.4± 3.28	4.1± 0.42	52± 3.02	2.1± 0.35	3.9± 0.42
P	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Hemoglobin datain the blood of patients in group I were lower compared to group II, which probably indicates less effective compensation for anemia, or slower rates of recovery of hematological parameters in children treated in the post-war period.

Children in both groups had the same average level of erythrocytes in the blood — 4,5×10^{12}/l, which indicates a certain leveling of the indicator after therapy, regardless of the period of hospitalization.

The average level of leukocytes in the blood of individuals in group I was lower compared to group II, which may reflect a less active course of concomitant inflammatory or infectious processes in children hospitalized after the start of the war, or a deeper suppression of leukopoiesis.

Summarizing the results obtained, it should be noted that the data of the general blood test in patients of group I demonstrate a less pronounced improvement in hematological indicators in the dynamics of treatment, which is probably due to the more difficult social and medical conditions during the war period. Group II, on the other hand, achieved better positive dynamics after the treatment, especially regarding the level of hemoglobin and leukocytes in the blood.

Our comparative analysis of biochemical blood parameters in children with anemia who were treated at different time periods allows us to identify possible differences in the metabolic and inflammatory status of patients in the observation groups (Tabl. 4.3).

Table 4.3

Study groups	ALT	AST	Urea	Creatinine	Direct Bill.	Indirect Bill.	Total Protein	Serum Iron	Calcium	CRP	Glucose
Group I	21.5±1.97	29.3±1.2	4.5±0.36	51.4±5.48	7.3±2.28	19.2±4.56	69.4±0.8	9.4±1.49	2.3±0.03	37±16.16	5.1±4.6
Group II	18±1.89	28.4±1.72	4.8±0.5	56.9±7.8	3±0.32	16.4±3.72	70.1±0.79	14.8±1.21	2.3±0.04	62.5±22.22	7±9.34
P	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	<0.05	>0.05	<0.05	<0.05

Results of biochemical blood analysis of patients in group I demonstrate significantly lower serum iron levels compared to group II. At the same time, serum iron levels are less than 5,4 µmol/l was registered in 50% of cases in the first group and only in 10% of patients in the second group ($P\varphi<0,05$). This difference indicates a deeper iron deficiency in the body of children hospitalized after the start of a full-scale war, which may be a consequence of both a chronic deficiency state and the influence of stress factors, poor nutrition, or late seeking medical help.

It should be noted that the relative risk of developing iron deficiency in children with anemia during active military operations compared to peacetime increases almost twice, and the odds ratio is almost 9, AR – 50,0%, RR – 2,3 (95% CI: 1,3-4,3), OR – 9,0 (95% CI: 4,2-19,3).

The average blood glucose level in patients in group I corresponded to normal values, while in group II it exceeded the upper limit of normal. Increased glycemia in group II may indicate concomitant endocrine disorders or metabolic adaptation characteristic of acute and chronic diseases.

The content of C-reactive protein in the blood was increased in both groups, but in patients of the second group it was significantly higher than in group I, which may indicate a more pronounced inflammatory component, or a transferred infectious pathology in children who were treated before the war. At the same time, increased CRP in group I also indicates the presence of an active inflammatory process, but of lower intensity (Fig. 4.12).

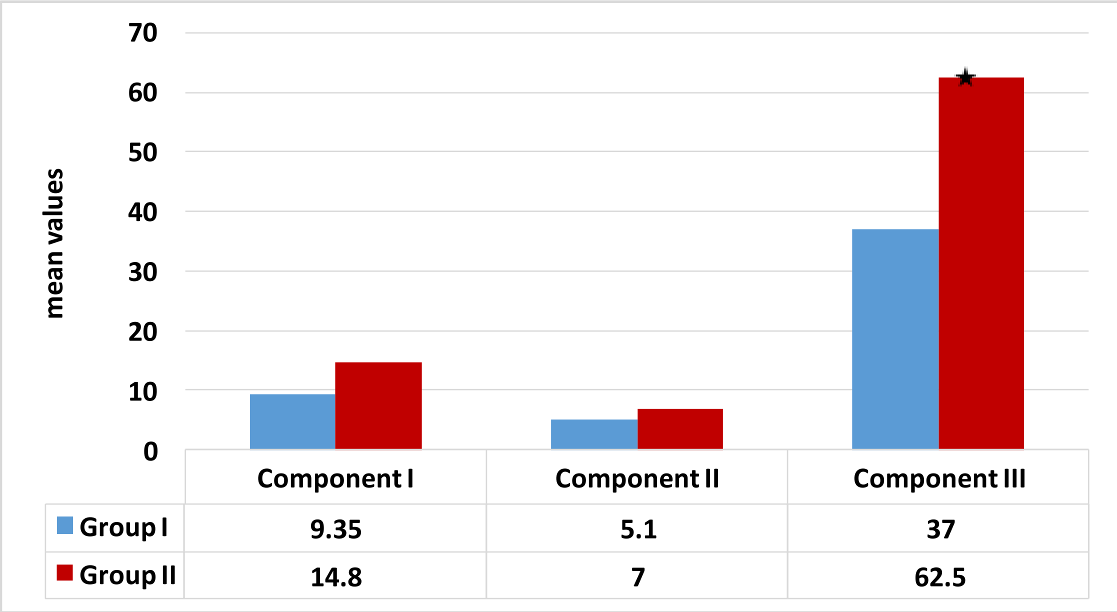


Fig. 4.12. Mean values of biochemical parameters in the comparison groups

Note: Legend: I – serum iron, II – blood glucose, III – C-reactive protein (CRP).

★- (P<0,05)

Therefore, the results of the above biochemical examination indicators of children in group I compared to group II demonstrate a greater iron deficiency with less pronounced inflammatory changes and normal carbohydrate metabolism, while patients in group II are characterized by higher levels of iron, glucose, and CRP in the blood, which may likely indicate other pathogenetic mechanisms of anemia or concomitant pathological processes.

Taking into account the negative impact of oxygen deficiency, which is characteristic of patients with anemia, primarily on the cardiovascular system, we analyzed the data of electrocardiological examination of children.

A comparative analysis of electrocardiographic parameters in children with anemia, who were divided into two groups depending on the time of hospitalization (pre-war and wartime), revealed significant differences in the frequency of pathological changes. Thus, normal ECG parameters were significantly more often registered in children of the second group compared to the first. In turn, pathological changes on the ECG were more often detected in patients of group I, which is also a statistically significant difference. This result emphasizes the increase in cardiovascular complications among children who are in martial law conditions, or with limited access to early diagnosis and prevention of anemia (Fig. 4.13).

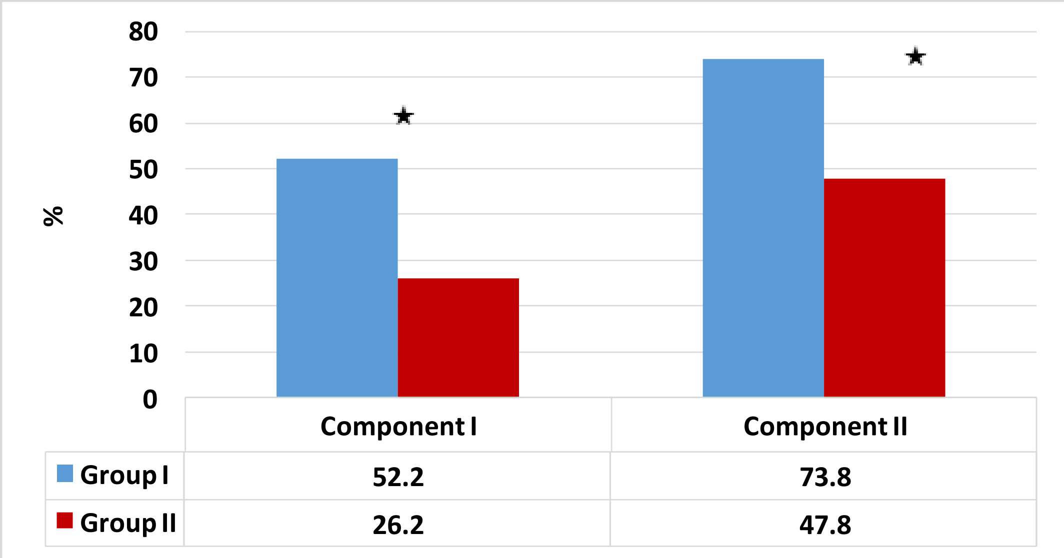


Fig. 4.13. Frequency (%) of detected abnormalities in electrocardiographic examinations

Note: Legend: Inormal ECG findings, II – pathological ECG changes.

★- ($P\varphi<0{,}05$)

Thus, the results demonstrate a deterioration in the ECG pattern in the post-war period, which may likely indicate a decrease in the functional state of the cardiovascular system in modern conditions, possibly due to stressful factors, delays in medical care, or severe forms of anemia.

The obtained data can be regarded as a negative trend in the somatic health of children with anemia during active military operations.

CHAPTER 5.
ANALYSIS AND GENERALIZATION OF RESEARCH

Diseases of the hematopoietic system, in particular anemia, remain an immediate problem in pediatrics. Anemia is one of the most common hematological disorders in children, detected at an early age. According to the literature, about 25% of the world's population suffers from anemia, and almost half of them are children under 5 years of age [1, 2]. The high prevalence of anemia among the child population is due to the anatomical and physiological immaturity of the hematopoietic system and its increased sensitivity to the influence of adverse environmental factors [3].

According to WHO experts, anemia affects about 1,62 billion people in the world, which is 24,8% of the population, of which almost half are preschool children (47,4%) [4, 5]. Simultaneously, about 20% of the population suffers from iron deficiency anemia, and its prevalence among young children reaches 50%. The highest incidence rates are recorded in developing countries, where anemia is diagnosed in 51% of children under 4 years of age and in 46% of children aged 5–12 years [7, 8].

At the same time, the problem of anemia in young children has significant social significance, as it can lead to disorders of physical development, metabolism, sleep, appetite and a decrease in emotional tone, which generally worsens the quality of life. Certain forms of anemia pose an immediate threat to life or cause a delay in physical and mental development [9]. Among the leading factors in the development of anemia in children are nutritional characteristics, living conditions and the environmental situation. Against the background of armed conflicts, such as the war in Ukraine, these factors are amplified: environmental pollution, food instability, psycho-emotional trauma, infectious risks and a general decrease in the quality of life have a significant impact on the health of children, forming threatening trends for public and environmental health [11-14].

Armed conflicts of the 21st century are often accompanied by large-scale humanitarian crises, where women and children become not only the main victims, but also direct targets of hostilities [7]. According to the UN, since the beginning of the full-scale invasion of Ukraine, 12,654 civilians have been killed and 29,392 injured, including 673 children. At least 790 attacks on medical facilities and 1,670 on educational institutions were recorded between February 2022 and February 2025 [52]. So, as of November 2024, 4,2 million Ukrainians have received temporary protection status in EU countries, among whom women account for 44,9% and children for 32,0% [53]. In addition, over 5,4 million people remain internally displaced [54, 55]. War contributes to the spread of diseases among refugees and creates the prerequisites for new outbreaks of infectious diseases, including tuberculosis, sexually transmitted infections, and enteric infections [56-59].

Thus, the war in Ukraine, which has been going on for over three years, significantly increases the risk of anemia in children both in frontline zones and in relatively safe regions. The health of the Ukrainian population, in particular children, is under significant threat, and the consequences of current events may have a long-term impact even after the active phase of hostilities has ended [66].

Based on this, war is an extraordinary factor that plays a leading role in the deterioration of the general condition of children, while studies of the impact of war on the characteristics of anemia in children are limited and remain a subject of scientific discussion. Therefore, the aim of our work was to analyze the features of the anemia in children of the Chernivtsi region before the start of the war in Ukraine and under martial law.

Research objectives:

1. To conduct a clinical and epidemiological analysis of the incidence of anemia among the child population in the pre-war period.
2. To assess the features of the course of anemia in children during martial law in Ukraine.

3. To conduct a comparative analysis of the features of the course of anemia in children before the war and during martial law.

To achieve the goal, we analyzed 113 medical records of children hospitalized in the Chernivtsi Regional Children's Hospital for anemia in the period from 2020 to 2024. Among the examined patients, boys accounted for 46,0%, girls – 54,0%. Most children (59,3%) were residents of the city, while 40,7% lived in rural areas. 78,7% of patients were organized (attended preschool or school institutions) and 21,3% were unorganized. Analysis of the social status of families showed that 31% of children were raised in families where both parents worked, 44,4% - in families with partial or full unemployment among parents, and 5% were orphans and half-orphans. In addition, 8% of patients were internally displaced persons as a result of hostilities. These data indicate a significant proportion of socially vulnerable families, which may affect the availability of medical care and the timeliness of diagnosis. In 73,5% of cases, the family history was uncomplicated, but in 26,5% a possible genetic predisposition to anemia was noted. The obstetric history in most cases was favorable, children were born mainly from the first or second pregnancy (30,97% and 21,24%, respectively). Also noteworthy is the low level of prolonged breastfeeding in the first 6 months of life (13.6%) as a possible factor in the development of deficient states [76-78].

The results of the analysis of clinical data of children hospitalized with anemia to the hematology department of the CRCH showed that the average duration of inpatient treatment was 14,7 ± 0,97 bed-days, with the majority of patients staying in the hospital from 6 to 15 days (over 65%), which corresponds to the average duration of hospitalization. In more than a third of children (45,13%), anemia was diagnosed for the first time during the current inpatient treatment, while in other cases it had a chronic course, which emphasizes the need for long-term clinical supervision.

The largest proportion of diagnoses of the examined children was iron deficiency anemia (63,16%), which corresponds to the data of the scientific literature [8, 9] and confirms their dominance among hematological pathologies of childhood. In the vast majority of cases, anemia had an uncomplicated course (97,3%) and was not accompanied by comorbidity (over 80%), which indicates a relatively isolated nature of the disease. At the same time, the presence of concomitant pathological conditions in approximately every fifth patient (21%) justifies the feasibility of a multidisciplinary approach to the management of such patients.

The results were processed using the software "STATISTICA" (StatSoftInc.) and ExcelXP for Windows. Depending on the type of distribution, parametric (Student's t-test) or nonparametric statistical methods were used. The data are presented as M ± SD (mean ± standard deviation). The probability of the null hypothesis was assessed at the significance level of $p<0.05$. The risk of the event was assessed taking into account the probability of the values of relative (RR), attributive (AR) risks and odds ratio (OR), as well as the determination of their confidence intervals (95% CI) [68-71].

To achieve the goal of the work, all patients were divided into two clinical comparison groups depending on the period of hospitalization. The first (I) group included 67 children who were inpatiently treated in the CRCH for anemia during the period of active hostilities (2022–2024). The second (II) group consisted of 46 patients hospitalized with a diagnosis of anemia in the pre-war period (2020–2022). Both groups were comparable in terms of basic clinical characteristics.

The results of demographic data of patients in group I versus those in group II indicate that children who came under observation after the outbreak of hostilities in Ukraine were more likely to live in rural areas (67,2% versus 54,3%) and were characterized by a slight predominance of females (58,2% versus 47,8%). The average age of patients at the time of hospitalization did not differ significantly: 9,2 ± 5,53 years in group I and 9,9 ± 5,76 years in group II ($P\varphi > 0,05$). The duration of the disease was also similar — 2,1 ± 3,9 years and 3,1 ± 4,7 years, respectively ($P\varphi > 0,05$). Socio-demographic analysis showed that in clinical group I (2022–2024), 31,6% of children had both working parents, while 22,8% grew up in families where both parents were unemployed, and another 15,5% were socially unprotected children. In clinical group II (2020–2022), only 20,0% of patients had both working parents, while 35,6% of children were raised in families where both parents did not work, and 7,4% were orphans or half-orphans. All differences were statistically insignificant (Pφ > 0,05).

Analysis of anamnestic data showed that blood group 0 (I) was somewhat more common in children who were hospitalized during active military operations (51% vs. 41,9%), and blood group B (III) (18,4% and 19,4%) had approximately the same frequency in both cohorts. The greatest difference concerned blood group AB (IV) (10,2% vs. 25,8%), the frequency of which decreased among pediatric patients hospitalized after the war began. Also, in clinical group I, anemia was more common in middle and high school-age children (26,6% vs. 20,5%), which may indicate the peculiarities of the course of the disease or a higher level of parental alertness. In contrast, in group II, diagnosis was more common at an older age (23,1% vs. 9,1%), which may indicate a later onset of symptoms or a delay in the diagnosis of this disease. According to the results, the most vulnerable age group in wartime was middle school children (11–14 years old). The probability of developing iron deficiency anemia during active hostilities in such patients was almost twice as high as in peacetime, with an odds ratio of 2,8 (95% CI: 0,9–8,2) and an absolute risk of 24,3%.

Comparative analysis of the time of anemia detection showed a statistically significant predominance of cases of recently diagnosed disease in group I (48,4% vs. 33,3%), while in group II chronic forms with a duration of more than 3 months prevailed (24,2% vs. 40,2%). This indicates the dominance of acute episodes of anemia in children hospitalized during the war, in contrast to the more chronic course in the pre-war period. Thus, among the clinical forms of anemia in hospitalized children, iron deficiency prevailed, which significantly more often occurred during the war (85% vs. 32,6%). At the same time, the majority of cases of congenital anemia were observed in the pre-war period (7,4% vs. 21,7%). The obtained data indicate a change in the etiological structure of anemias against the background of the war and emphasize the need for an etiologically oriented approach to diagnosis. At the same time, in war conditions, the risk of developing iron deficiency anemia increases almost 4 times, and the odds ratio is almost 12, AR – 50,0%, RR – 3,9 (95% CI: 2,9-5,3), OR – 11,7 (95% CI: 5,8-23,4).

It should be noted that when conducting a comparative analysis, we found a difference by category of symptomatic treatment received before hospitalization, which was more common in group II (7,5% vs. 23,9%, ($P\varphi<0,05$)). In contrast, group I was dominated by patients who did not receive treatment before hospitalization (52,2% vs. 39,2%). The use of specific therapy before admission was similar in both groups (40,3% and 36,9%, respectively), which indicates relatively equal access to targeted treatment.

Analysis of clinical manifestations of anemia, namely the severity of its course, showed that in children hospitalized during active hostilities, almost half of the cases had severe and moderate forms of the disease (49,9%), compared with 34,8% in patients hospitalized in peacetime ($P\varphi<0,05$). The relative risk of developing severe and moderate anemia during wartime compared to peacetime increases by 1,4 times, and the odds ratio is almost 2 (AR – 15,0%, RR – 1,4 (95% CI: 0,9-1,9), OR – 1,9 (95% CI: 1,1-3,3)). Our results indicate a more pronounced clinical picture of anemia in children hospitalized after the start of the war, which may indicate limited access to medical care, diagnostics or nutrition in conditions of limited opportunities, which requires further study.

It should be noted that when comparing the results of instrumental and laboratory tests, namely the complete blood count (CBC) upon admission, we found that children in group I had lower erythrocyte and reticulocyte counts (3,9±0,14 versus 4,3±0,13 and 1,3±0,41 versus 5,9±1,01, respectively), which may indicate a deterioration in the body's adaptation to anemia and possible impaired bone marrow function in war conditions. In contrast, the results of patients in group II demonstrate a higher level of regeneration, which indicates better compensation for the anemic state. Summarizing the results obtained, it should be noted that the data of a repeated complete blood count in patients in group I show a less pronounced improvement in hematological indicators during treatment, which is probably due to more difficult social and medical conditions during active hostilities. In contrast, group II demonstrated better positive dynamics after treatment, especially regarding the level of hemoglobin and leukocytes in the blood. Analysis of biochemical blood parameters revealed significant differences between the comparison groups. Thus, in patients of group I, the serum iron level was significantly lower, with a profound deficiency in 50% of cases, which may indicate the presence of chronic nutritional deficiency due to poor nutrition or late seeking medical care. The relative risk of iron deficiency during the war increases by half, and the odds ratio is almost 9, AR – 50,0%, RR – 2,3 (95% CI: 1,3-4,3), OR – 9,0 (95% CI: 4,2-19,3). In contrast, in patients of group II, an increase in glucose was observed, which may indicate metabolic disorders (5,1 mmol/l versus 7,0 mmol/l). Elevated levels of C-reactive protein in both groups indicate an active inflammatory process, with more pronounced inflammation in group II (37,3 mg/l versus 62,5 mg/l). In turn, analysis of ECG data indicates a worsening of the picture in the period after the start of hostilities (73,8% versus 47,8% of individuals), which probably indicates a decrease in the functional state of the cardiovascular system due to stress factors, delayed medical care, or more severe forms of anemia.

The data we obtained can be regarded as a negative trend in the physical health of children during active military operations.

CONCLUSIONS

1. The clinical and epidemiological characteristics of children with anemia suggest the development of this disease in patients born from the first and second pregnancies, with a relatively low level of long-term breastfeeding (more than 6 months), from families where at least one of the factors of social disadvantage is recorded - unemployment of one or both parents, or lack of parental care (76,32%).

2. During the Russian-Ukrainian war, there was a significant increase in the incidence of iron deficiency anemia among children, especially patients of middle school age (11–14 years) (13,2% during the war and 5,1% in peacetime), the probability of developing the disease in such patients almost doubled, with an odds ratio of 2.,8 (95% CI: 0,9–8,2) and an absolute risk of 24,3%.

3. In children who became anemic during active military operations, the risk of developing moderate and severe anemia increases almost twice: (AR – 15,0%, RR – 1,4 (95% CI: 0,9-1,9), OR – 1,9 (95% CI: 1,1-3,3)).

4. The war in Ukraine increases the risk of iron deficiency anemia in children by almost 4 times, and the odds ratio is almost 12, even in a relatively safe region of the country (AR – 50,0%, RR – 3,9 (95%CI: 2,9-5,3), OR – 11,7 (95%CI: 5,8-23,4)).

RECOMMENDATIONS FOR FURTHER USE

To improve the prediction of the type, severity, and age of development of anemia in children during wartime, the increased influence of a number of maternal risk factors for this disease should be taken into account, in particular:

1. During active military operations in the country, more severe forms of the disease are registered much more often in pediatric patients, which are diagnosed with a significant delay in time in conditions of limited resources.
2. When anemia is suspected in children during war, it is necessary to considersocio-demographic data and the child's age, since the probability of developing iron deficiency anemia during active hostilities in middle school-age patients (11–14 years old) is twice as high compared to peacetime.

To improve the prediction and prevention of the development of childhood anemia during wartime, the increased influence of social factors, environmental adversity, and stress on the child should be taken into account.

Comprehensive consideration of these factors will allow for better diagnosis and treatment of children with anemia.

Analysis of passing the academic integrity test.

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