

MICROCYTIC ANEMIA

Causes, Pathology, and Differences from Other Types of Anemia:

A General Review

Authors: **Mahmudov Asadbek**

Muhammadiyah Mahlioxon

Oripov Aziz

Rixsiboyeva Robiyabonu

Zohidov Rahmatulloh

Supervisor: Maksumova Munira Abduganiyeva

Abstract. This article discusses iron deficiency anemia, its causes, etiology, pathology, and diagnostics, as well as its differences from other types of anemia. Before comparing microcytic anemia with other types, a brief overview of these other anemias is provided.

Keywords: anemia, microcytic, macrocytic, hemolytic, hemoglobinopathy, erythrocyte, hypochromic, hyperchromic, hematocrit, iron deficiency, pregnancy and anemia, B12 deficiency.

Introduction

Anemia is a disease characterized by an insufficient number of red blood cells or hemoglobin in the blood or their inability to perform their function fully. It remains one of the most widespread diseases globally, particularly among children and women. Like other diseases, anemia affects patients' work capacity and quality of life and can sometimes lead to death. Thus, understanding the causes, etiology, and pathology of anemia is crucial for effective treatment. There are several types of anemia, and recognizing their differences is vital for diagnosis and treatment.

Classification

1. Microcytic or hypochromic anemia - it is also referred to as "iron deficiency anemia" because it arises due to a deficiency of iron in the body. In this type of anemia, the number of erythrocytes may be normal, but their size is small, which is due to a low amount of hemoglobin. This type of anemia is primarily found in economically underdeveloped regions, particularly in Africa, Afghanistan, Angola, and similar areas.

2. Macrocytic or hyperchromic anemia - the amount of hemoglobin exceeds the normal level; however, the number of erythrocytes is low or immature. Additionally, this type of anemia is characterized by the large size of erythrocytes.

The article provides general concepts about macrocytic anemia.

Literature Analysis and Methodology

This article was written based on the World Health Organization (WHO), articles from the PubMed database, and medical textbooks (see references). The "Keyword Mapping" and "snowballing" methods were used for data collection. The compared data are presented in tabular form.

Mikrocytic anemia: etiology, pathology, and origins

The human body contains about 2.5-5 grams of iron. Approximately 60% of this amount is found in hemoglobin. As is known, hemoglobin is composed of two components: a complex that holds iron, called heme, and a protein component, globin. Typically, a single globin can hold four heme groups, resulting in the formation of hemoglobin, which is the norm.

When there is an iron deficiency in the body, iron deficiency anemia occurs (since, as mentioned above, iron is one of the main components for the synthesis of hemoglobin). Due to the lack of heme, the size of red blood cells decreases, and their color becomes pale (hence it is also referred to as 'hypochromic' anemia), leading to a reduced oxygen-carrying capacity compared to normal. This, in turn, results in hypoxia and can cause headaches, dizziness, palpitations, hair loss, brittle nails, smoothing of the tongue, and changes in taste perception due to insufficient oxygen reaching the brain. Due to the lack of oxygen in muscle tissues and throughout the body, the processes of energy metabolism do not proceed to completion, causing weakness, muscle pain, and constant fatigue.

Iron deficiency can be classified into several types based on its origins:

- Related to nutritional deficiencies (lack of iron, vitamin B12, or vitamins A and K);
- Caused by inflammation and other diseases;
- Resulting from genetic changes (such as thalassemia and hemolytic anemia).

Nutritional Deficiency

There are hematopoietic nutrients that must regularly enter the human body, including vitamins A, B12, K, and iron. A lack of sufficient intake of these nutrients, their sudden loss in large amounts, or their continuous gradual loss (due to parasites, various infections, or an improper diet) disrupts erythropoiesis. As a result, anemia develops. According to WHO data, iron deficiency anemia mainly occurs in children and pregnant women. This is due to several

factors in women, such as a high demand for weight loss, the menstrual cycle, and pregnancy (according to "Measurement of soluble transferrin receptor in serum of healthy adults," 9.5% of women with normal blood parameters were found to have iron deficiency, whereas this figure was only 1.5% among men).

Children often inherit this type of anemia from their mothers. If a mother has nutrient-related anemia, there is a high probability that her child will also have it. Therefore, it is crucial first to determine the reason for the nutrient deficiency. Most often, it stems from an improper diet or insufficient nutrient intake. According to the National Institutes of Health website:

Age	Males	Females
9-13 years	8mg	8mg
14-18 years	11mg	15mg
19-50years	8mg	18mg
51+years	8mg	8mg

The daily food intake should contain the following amounts of iron.

It is important to note that in women between the ages of 14 and 50, the need for iron significantly increases. This is because during this period, menstrual cycles and pregnancy occur. After the age of 50, the requirement decreases due to menopause.

Inflammation and Associated Conditions

When an inflammatory process is occurring in the body, erythropoiesis (the production of red blood cells) is disrupted, and the lifespan of erythrocytes is also shortened. This happens because immune responses directed at infections interfere with iron metabolism and suppress the activity of erythropoietins. As a result, anemia develops.

Another common cause is parasites. Hemophagous parasites, such as *Ancylostoma duodenale*, continuously damage the intestinal wall and feed on blood, leading to internal bleeding in the gastrointestinal tract. Similarly, *Schistosoma mansoni*, which belongs to the schistosomal group, is also a hemophagous parasite that can cause anemia.

Additionally, loss of appetite associated with diseases such as tuberculosis, enterobiasis, and ascariasis can also lead to the development of anemia.

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Origin and Pathology of Hemolytic Anemia

In hemolytic anemia, erythrocytes break down earlier than normal. This can be caused by internal or external environmental factors. Normally, healthy erythrocytes function for about 120 days before being broken down in the liver. However, in this type of anemia, erythrocytes are destroyed prematurely, and the body is unable to produce enough new red blood cells to compensate. This leads to anemia and a number of related complications.

Hemolytic anemia is divided into two groups based on its origin and mechanism:

Hereditary (genetic) hemolytic anemia: This is an autosomal recessive genetic disorder in which abnormal globins are synthesized in the body, causing erythrocytes to assume a sickle shape. Therefore, this type of anemia is also referred to as "sickle cell anemia" or "thalassemia." The disease is classified into α - and β -types. Specifically, a mutation in a single gene (most often the substitution of valine for glutamine in the β -chain) leads to the synthesis of abnormal proteins. As a result, erythrocytes are targeted and destroyed by the immune system. In addition, aggregation of these cells can occur, which may lead to heart defects.

Acquired hemolytic anemia: This form arises due to various factors such as medications, infections, autoimmune reactions, or toxins. In this case, the immune system mistakenly recognizes red blood cells as foreign and destroys them.

The breakdown of erythrocytes can occur in two main ways:

1. Intravascular hemolysis – breakdown within the blood vessels, typically due to autoimmune reactions or various infections.
2. Extravascular hemolysis – breakdown mainly occurs in the liver and spleen, usually as a result of immune system activity or structural abnormalities of the erythrocytes (caused by hereditary factors).

Diagnostics

During the initial examination, attention should be paid to the fact that patients with anemia may exhibit short and rapid breathing, arrhythmia, and in some cases, discoloration (bruising) at the tips of the fingers and toes. These symptoms occur due to the role of hemoglobin in gas exchange. When tissues do not receive an adequate supply of oxygen, such symptoms develop.

In diagnosing microcytic anemia, the size of erythrocytes and the amount of hemoglobin they contain are used as key indicators.

To determine erythrocyte size (MCV – Mean Corpuscular Volume), the hematocrit value must be divided by the number of erythrocytes (RBC) in the blood. Normally, the MCV results range between 80–100 fL. In anemia, it typically falls below 72 fL.

Hematocrit: The normal range is 40–54% in men and 36–48% in women. If anemia is caused by inflammatory processes, this value tends to increase. In nutritional deficiency (ND), it usually remains relatively unchanged.

RBC (Red Blood Cell count): The number of erythrocytes in one microliter of blood; normally, 4.7–6.1 million in men and 4.2–5.4 million in women. If anemia is caused by inflammation, the RBC count decreases. In nutritional deficiency, it tends to increase.

Hemoglobin: The amount of hemoglobin (in grams) per liter or deciliter of blood (1 liter = 10 deciliters). Normal values are:

Men: 132–166 g/L, Women: 116–150 g/L. Children (under 5 years old): 115–155 g/L. If anemia is due to inflammatory processes, hemoglobin levels decrease. In nutritional deficiency anemia, hemoglobin levels may be as follows:

Indicators	Normal Range	Anemia(Nutritional Deficiency)
Hemoglobin(Hb)	For men:135-166 g/L	Hb<80 g/L
	For women:116-150 g/L	Hb<80 g/L
	For children aged 1-5 years: 115-155 g/L	Hb<70 g/L

Other indicators change accordingly. That is, due to the reduced efficiency of each erythrocyte in binding oxygen, the RBC value significantly increases. However, because the size of the red blood cells decreases, their increased number does not significantly affect the hematocrit level.

In hemolytic anemia, an increase in the number of reticulocytes (blood-forming cells) can be observed, as the body attempts to compensate for the lost erythrocytes. An increase in bilirubin levels is also noted. These analyses help in diagnosing hemolytic anemia.

Origin of Macrocytic Anemia

Before moving into the discussion, let us briefly explain macrocytic anemia. This type of anemia is characterized by the enlargement of erythrocytes. In blood tests, it is identified by an MCV (Mean Corpuscular Volume) value that is higher than normal. This type of anemia develops due to a deficiency of vitamin B12. As a result, erythrocytes are unable to mature properly, and their number decreases, while the hemoglobin concentration increases. Therefore, this condition is also referred to as "pernicious anemia" or "hyperchromic anemia."

Since vitamin B12 is primarily found in animal products, this type of anemia most often occurs in vegetarians and individuals with liver diseases. Additionally, it is commonly seen in the elderly and in those who have undergone stomach surgeries. In some cases, the disease can also be caused by various medications. For example, macrocytic anemia can develop under the influence of methotrexate, sulfasalazine, and antiepileptic drugs. Furthermore, macrocytic anemia may occur alongside conditions such as Addison-Biermer disease, SPRUE, and intestinal infestations. Therefore, a broad and comprehensive approach to diagnosis and treatment is necessary.

This type of anemia is classified into two forms:

1. Megaloblastic anemia – associated with disrupted DNA synthesis within cells, with vitamin B12 deficiency being the primary cause. In this case, although the erythrocytes are enlarged, they remain immature.
2. Non-megaloblastic anemia – occurs without disruption of DNA synthesis and is usually associated with liver diseases, alcoholism, and similar conditions.

Discussion

Above, we reviewed several types of anemia. The main differences between them lie in their origins, prevalence, and mechanisms of development. For example, microcytic anemia primarily occurs in children and women, while macrocytic anemia is more common among vegetarians and the elderly. This is related to their lifestyles and physiological characteristics. During pregnancy, women transfer most of their vitamins and essential nutrients to the developing fetus. If these reserves are not replenished, it can lead not only to anemia but also to the development of other related diseases. Moreover, the newborn may inherit anemia from the mother.

The development of the disease is also influenced by geographical location and natural environmental conditions. For instance, thalassemia is widespread in African countries. This is because malaria parasites cannot reproduce in sickle-shaped erythrocytes. Thus, for Africans, thalassemia serves as a form of adaptation to resist malaria. However, it would be more accurate to call it natural selection rather than adaptation, because over time, individuals with normal erythrocytes tended to die out in those regions, while those with thalassemia survived and multiplied, given that it is a hereditary condition. Now, regarding the differences among anemias: although their causes and development mechanisms vary, anemias often present with very similar symptoms. Therefore, laboratory tests and careful attention from physicians are crucial to identify the exact cause.

For example:

Microcytic anemia typically arises from nutritional deficiencies, inflammation, or genetic factors; Macrocytic anemia mainly results from disruptions in protein biosynthesis or vitamin B12 deficiency. Based on the review above, we can distinguish: In inflammation-related anemia, the number of leukocytes increases; In hemolytic anemia, bilirubin levels rise; In nutritional deficiency anemia, erythrocyte size decreases while their number increases; In macrocytic anemia, erythrocytes are larger but immature, and their number decreases. Often, vitamin B12 deficiency is accompanied by iron deficiency (due to poor diet or insufficient intake). In such cases, microcytic anemia develops. However, if the body has enough iron but lacks vitamin B12 (for instance, in vegetarians), macrocytic anemia occurs.

Conclusion

The types of anemia, along with their causes and mechanisms of development, have a significant impact on the overall health of the body. Microcytic and macrocytic anemias develop through distinct mechanisms and causes. Microcytic anemia primarily results from iron deficiency; Macrocytic anemia occurs due to a deficiency of vitamin B12, leading to the enlargement and impaired maturation of erythrocytes. Regardless of the type, it is extremely important to diagnose and treat anemia in a timely manner.

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