Anemia in gastrointestinal tract diseases

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Abstract

Aim: Anemia is one of the most important symptoms associated with several pathologies of the gastrointestinal tract. The aim of this study was to assess the level and types of anemia among patients with different diseases of the gastrointestinal system in Albania.
Methods: This study included 100 patients with various pathologies of the gastrointestinal tract, who were admitted at the Gastroenterology and Hepatology Service of the University Hospital Center "Mother Teresa" in Tirana, Albania. All of the patients were examined and treated during the period February-June, 2012.
Results: The infections/inflammation of the gastrointestinal tract accounted for 41% of the overall patients included in this study. In this group, 82% of the patients had erythropenia, 15% had normal values of erythrocytes and 3% had an increased number of erythrocytes. Based on hemoglobin levels, 60% of the patients had minor anemia, whereas moderate and severe anemia comprised 20% of cases each.
Conclusion: In the Albanian context, we showed that the most common cause of chronic anemia consists of gastrointestinal diseases, and this fact explains why the majority of the patients with anemia are referred to gastroenterologists.

Keywords: anemia, erythrocytes, gastrointestinal diseases.

Introduction

Anemia is one of the most important symptoms associated with several pathologies of the gastro-intestinal tract (TGI) (1). Hence, anemia may derive from dietary deficiency, mal-absorption, or acute and chronic bleeding (1). The World Health Organization (WHO) has standardized the diagnostic criteria of anemia determining reference values of hemoglobin level in the blood, depending on age and sex of individuals (1). Based on these criteria established by the WHO, individuals are considered anemic when the hemoglobin level in the blood is less than 13 g/dl for males and 12 g/dl for females (1).

On the other hand, according to the definition of anemia, the classification of anemia is based on morphological criteria (microcytic, macrocytic and normocytic anemia) and pathogenic anemia (regenerative and hypo-regenerative) (1). Laboratory tests which establish anemia consist of some basic and simple methods including a complete blood test, routine biochemical tests, up to more specific tests such as the level of vitamin B_{12}, folic acid, the number of reticulocytes, the examination of bone marrow, the level of erythropoietin, the transferine soluble receptors, hepcidine level, and the like (2). Various algorithms of anemia have been proposed as a hierarchical and logical manner to establish diagnosis promptly, combining medical history with physical examination, laboratory tests, bone marrow examination and additional examinations (2).

Erythrocytes and digestive system are closely linked since the beginning of life. Gastrointestinal system plays an important role in the production of erythroid predecessors in intrauterine life. Liver is the only source of red blood cells until the 18^{th} week of pregnancy. Subsequently, spleen and bone marrow produce eritropoesen, but liver continues to play a role in a small percentage until the 6^{th} week after birth. Adult esophagus, stomach, intestines and liver are involved in the pathogenesis of various types of anemia, caused by dietary deficiencies, bleeding or chronic inflammation (2).

Some diseases of the esophagus (varicose veins, diverticuls diafragmal hernia, tumors, ulcers, esophagitis and Mallory-Weiss syndrome) can cause acute and chronic bleeding (3). The stomach plays a crucial role in the protection of vitamin B_{12} since it is absorbed in the final part of ileum. The stomach also contributes to the maximum absorption of iron in enterocite reducing iron from $Fe^{3}+$ in $Fe^{2}+$. Also, the stomach may be the source of bleeding in the boil ulcer, gastritis and tumors, caused by aspirin and anti-inflammatory non-steroids (3,4). Iron absorption in the duodenum is a very complicated process. Mucosa of the small intestine plays an essential role in the absorption of foliates. Vitamin B_{12} is absorbed in the terminal ileum, that is the reason why some inherited or acquired gastrointestinal pathologies, as well as surgical removal of parts of TGI, can produce anemia by mal-absorption (3,4).

Inflammatory bowel diseases are a frequent cause of anemia in chronic diseases (4). Chronic bleeding is an important sign that suggests the diagnosis of malignant and benign injuries (such as diverticuls) in the colon and rectum.

Splenomegaly is a common cause of chronic hemolysis, whereas more rarely, Zieve's syndrome is the cause of acute hemolytic crisis. Likewise, the liver plays an essential role in the control of iron metabolism through hepcidine, which represents the hormone that controls the metabolism of iron and is produced in hepatocytes (5).

Links between anemia and digestive system are quite strong and numerous. Because of this, there is a need of close cooperation between hematologists and gastroenterologists and hepatologists for a better and deeper understanding of the pathogenesis of this phenomenon.

The most common causes of chronic anemia are the gastrointestinal diseases, and this fact explains why the majority of patients with anemia are referred to a gastroenterologist (6).

The classification of anemia can be based on three different viewpoints: in pathogenesis, erythrocyte morphology and clinical signs. Pathogenic mechanisms that lead to anemia include the insufficient

production and loss of red blood cells as a result of bleeding or hemolysis. Based on these pathogenic mechanisms anemia is classified into two types: (i) hypo-regenerative anemia, when production of bone marrow decreases as a result of damage of its function, reduction of the number of precursor cells, reduction of bone marrow infiltration or lack of nutrition (6); (ii) regenerative anemia when bone marrow responds to a reduction of the number of red blood cells by increasing their production (6).

Measurement of reticulocytes is an important diagnostic tool in the differentiation of anemia for which there is a good response to bone marrow, in comparison to anemia in which there is a reduction of their production from bone. Concentration of reticulocytes provides direct information about bone marrow response toward anemia display. This information is especially necessary when the MCV is normal (7).

However, in routine clinical practice, the most frequently used classification is based on the assessment of laboratory parameters of hemogram. Based on the values of MCV, anemia conditions are classified as: microcytic (MCV<82fL), normocytic (MCV=82-89 fl), and macrocytic (MCV>98fL) (8,9). MCV is closely linked to MCH, which expresses the average amount of Hb in red blood cells measured in pictogram (normal values:27-32 PCG). Consequently, MCV and MCH are reduced at the same time (hypochrome microcytic anemia), or increased at the same time (hyperchrome macrocytic anemia). MCH concentration (MCHC) is the concentration of hemoglobin in each red blood cell expressed as a percentage (normal value: 32%-36%); its fluctuations are very small even in cases when hypochromia is present. MCHC grow only in certain rare diseases such as the inherited spherocytosis; therefore, the use in clinical practice of MCHC has a very limited value. But, it should always be kept in mind that MCV expresses the average value and, as a result, it does not give information about the homogeneity of the erythrocytes. In order to solve this problem, hematological analyzers present the distributional curve of erythrocytes, accompanied by the following distribution index: RDW (erythrocyte distribution width), the normal values of which are 10%-14%. A simple blood test conducted with automatic analyzer provides immediate information about a mycrocytic anemia. Evaluation of RDW helps in the differential diagnosis of anemia against thalassemia, compared to the inadequate level of iron. Hence, RDW is normal in thalassemia, whereas the opposite occurs in microcytic anemia, where RDW is found at a high level; thus, a RDW>15 is a sign of anemia caused by iron deficiency (10,11).

In recent years, it is given a greater importance to clinical differential diagnosis between chronic anemia and iron deficiency anemia, as well as evaluating plasma levels of trasferine solubel receptors. Hence, the blood level of trasferine soluble receptors found in adults in iron deficiency anemia, while its level does not change in the anemia from chronic diseases (12,13). Measurement of serum ferritine and erythrocyte zinc-protoporphyrin can also be used as a tool for differential diagnosis between these two types of mycrocytic anemia.

Microcytosis accompanied by normal levels of serum ferritine provides information about the diagnosis of hereditary diseases, such as thalassemia. If there is no evidence of hereditary microcytosis, other causes should be sought, which lead to a gained microcytosis including anemia resulting from chronic diseases, or sideroblastic anemia. Normal levels of RDW provide information on the first type of anemia, while a high level of RDW suggests the second type of anemia.

Anemia can also be classified based on its clinical presentation as acute anemia (usually caused by bleeding or hemolysis), or chronic anemia (13,14).

Methods

This study included 100 patients with various pathologies of the gastrointestinal tract, who were admitted at the Gastroenterology and Hepatology Service of the University Hospital Center “Mother Teresa” in Tirana, Albania.

All of the patients were examined and treated during the period February-June, 2012. The criteria of being part of this study was the confirmation of the presence of TGI pathology and the presence of anemia (Hb<12 mg/dl for women and Hb<13 mg/dl for men). Exclusion criteria were cases where the tract pathologies were a secondary disease (i.e., cases where the pathology was associated with other illnesses and not TGI) and Hb values within the norm. The patients in this study were divided by sex, the number of erythrocytes, the value of Hb, MCV, MCH, MCHC, total bilirubine, direct bilirubine, AST and ALT.

For determining the parameters of hemogram we used blood samples drawn with K3EDTA, whereas for biochemical parameters we used lithium/heparin tubes. The patients were grouped into four diagnoses performing also the etiological classification of anemia: (i) infection/inflammation of TGI; (ii) tumors TGI; (iii) ulcers of TGI, and; (iv) melena and hematemesis.

For all patients included in this study we assessed anemia based on the number of erythrocytes, the Hb level, Hct and erythrocyte constants calculated from them. Thus, based on the level of Hb, we classified anemia as follows:

- Minor anemia: 9.5-13.0 g/dL
- Moderate anemia: 8.0-9.5 g/dL
- Severe anemia: <8.0 g/dL

Results and Discussion

Anemia in infections / inflammation of TGI

Distribution of anemia in infections/inflammation of TGI is presented in Table 1. This group accounted for 41% of all diagnoses that were observed in this study, accounting for the largest percentage of them. In this group, there was observed that 82% of the patients had erythropenia, 15% had normal values of erythrocytes and 3% had an increased number of erythrocytes. Hence, the number of red blood cells cannot be an indicator of anemia, because anemia can be caused in cases of reduced number of red blood cells, as well as in cases when their number is increased.

Based on the values of Hb, 60% of the patients had minor anemia, whereas moderate and severe anemia comprised 20% of cases for each. This is supported by literature data in which it is stated that inflammation anemia is mild and in a small number of cases it is moderate (6). Given the values of MCV, 56% of the patients had normocytic anemia, whereas 12% had macrocytic anemia. Our findings in this regard are supported by the literature, which states that anemia of inflammation is normocytic and in a small percentage microcytic (6,7).

Looking at the MCH values, 56% of patients had normochrome anemia, and only 3% had hyperchrome anemia.

Table 1. Distribution of anemia in infections/inflammation of TGI

Characteristic	Percentage
Erythrocytes <4.2 million/mm^3	82%
Erythrocytes 4.2-5.8 million/mm^3	15%
Erythrocytes >5.8 million/mm^3	3%
Hb <7 mg/dl	20%
Hb 7-9 mg/dl	20%
Hb >9 mg/dl	60%
MCV<80 fl	32%
MCV 80-97 fl	56%
MCV>97 fl	12%
MCHC<31.5 g/dl	41%
MCHC 31.5-35.0 g/dl	56%
MCHC>35.0 g/dl	3%

Anemia in TGI tumors

Distribution of anemia in TGI tumors is presented in Table 2. These pathologies comprised the second most frequent group (23% of the overall pathologies).

Table 2. Distribution of anemia in TGI tumors

Characteristic	Percentage
Erythrocytes <4.2 million/mm^3	74%
Erythrocytes 4.2-5.8 million/mm^3	26%
Erythrocytes >5.8 million/mm^3	0%
Hb <7 mg/dl	22%
Hb 7-9 mg/dl	35%
Hb >9 mg/dl	43%
MCV<80 fl	57%
MCV 80-97 fl	43%
MCV>97 fl	0%
MCHC<31.5 g/dl	48%
MCHC 31.5-35.0 g/dl	48%
MCHC>35.0 g/dl	4%

About 74% of the patients with tumors had TGI erythropenia and 26% had normal values of erythrocytes. Given the values of Hb, it can be concluded that 43% of the patients had mild anemia, 35% had secondary anemia and the remaining 22% had severe anemia. Regarding the MCV values, 57% of the cases had microcytic anemia and 43% had normocytic anemia. In this group of patients, the anemia was hypochrome and normochrome at same levels (44%), whereas hyperchrome anemia constituted only 4% of the group.

Anemia in TGI ulcers

TGI ulcers accounted for the third most frequent group constituting 22% of the overall pathologies in this study. In this group of pathologies, only 9% of the patients had a normal number of RBC, whereas the remaining 91% had erythropenia. Based on the values of Hb of patients, 41% had mild anemia, 41% displayed moderate anemia and only 18% of the cases had severe anemia. The most prevalent type was the normocytic anemia accounting for 82% of the cases, whereas the remaining 18% had hypochrome anemia. Overall, 59% of the patients with TGI ulcers had normochrome anemia, 32% had hypochrome anemia and 9% had hyperchrome anemia.

Anemia in cases with melena and/or hematemesis

Melena and hematemesis constituted 16% of the overall pathologies of TGI, which were associated with anemia. All patients who had melena and/or hematemesis exhibited erythropenia. About 50% of the cases had severe anemia, 19% had secondary anemia and 31% has mild anemia. Normocytic anemia was the most frequent type of anemia (in 69% of the cases), followed by the microytic anemia (25% of the cases) and next macrocytic anemia (only in 6% of the cases). In 50% of the cases, there was evidence of normochrome anemia, in 38% of the cases there was hypochrome anemia and in 22% of the cases it was hyperchrome anemia.

Conclusions

Based on values of Hb, anemia is classified into mild, moderate and severe anemia. In our study, the most common type of anemia was the mild anemia, which accounted for 47% of the overall cases with anemia, whereas the other two types of anemia had a similar (lower) percentage (29% and 24% of the cases, respectively). Based on the MCV values, we were

able to assess the type of anemia (microcytic, normocytic, and macrocytic). Based on this, we concluded that 36% of the cases had microcytic anemia, 58% had normocytic anemia (the largest percentage), while macrocytic anemia constituted the least frequent type of anemia (6%).

About 44% of the patients had values below the rate of MCH, 56% had normal values of MCH and 2% had values higher than the normal range.

Anemia is a syndrome, not a disease and, as such, its etiology should be studied in depth and recommended treatment should be directed to treat the basic disease that has caused the anemia, and should not have only the objective to increase the hemoglobin level in the blood. In order to evaluate anemia, we should probably pay more attention on simple tests such as complete blood rather than more complex tests. In patients with anemia, laboratory data are often insufficient to reveal its true cause. In such cases, these data should be supplemented with other tests, to better understand the presence of various gastrointestinal or oncologic diseases.

Conflicts of interest: None declared.

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