

ASSESSMENT OF ANEMIA IN CORRELATION WITH INFLAMMATORY STATUS IN PATIENTS WITH INTESTINAL TRANSIT DISORDERS

Cristina Voicu¹, Sorin Rugină²

¹Sfântul Apostol Andrei” Emergency County Clinical Hospital, Clinic Medical I, Constanța

²Ovidius” University of Medicine, Constanța

Corresponding author: Cristina Voicu, dr_cristinavoicu@yahoo.com

Abstract

The intestinal transit disorders are polymorphic clinical manifestations requiring complex differential diagnosis and a multidisciplinary medical team.

A major challenge for the clinician is the differentiation of patients with organic suffering versus functional disorder.

Anemia is the most common extra-digestive manifestation of intestinal inflammatory diseases.

We have evaluated biologically and by imaging patients with diarrhea and alternating diarrhea/constipation without including infectious causes. We plan to determine in these patients the status and type of anemia, as well as its correlation with local and systemic inflammation.

Key words: anemia, intestinal inflammation, chronic diarrhea

Rezumat

Tulburările de tranzit intestinal sunt manifestări clinice polimorfe care necesită diagnostic diferențial complex și echipă medicală multidisciplinară. O provocare majoră pentru clinician constă în diferențierea pacienților cu suferință organică versus tulburare funcțională.

Anemia reprezintă cea mai frecventă manifestare extradigestivă din cadrul bolilor inflamatorii intestinale. Am evaluat biologic și imagistic pacienții cu diaree și alternanță diaree/constipație cu caracter cronic, fără a include cauzele infecțioase. Ne propunem să determinăm la acești pacienți stadiul și tipul anemiei, precum și corelarea acesteia cu inflamația locală și sistemică.

Cuvinte cheie: anemie, inflamație intestinală, diaree cronică



INTERNAL MEDICINE

Original papers

Introduction

Chronic diarrhea is defined in the medical terminology as the presence of at least three stools of low consistency with a duration of minimum four weeks.

Elucidation of the cause of the transit disorders is a serious challenge as a very wide specter of conditions belonging to several specialties have them as a component of the clinical presentation.

An important aspect in clinical practice facing the internal medicine specialist is the differentiation of patients with organic conditions such as inflammatory bowel diseases or colorectal neoplasia of those with irritable bowel considered a functional condition.

Inflammatory bowel diseases commonly associate during the evolution intestinal and extra-intestinal manifestations. The extra-intestinal manifestations are generally closely related to the activity of the bowel disease and can be simultaneous with the intestinal symptoms or can precede them. The presence of extra-digestive symptoms is commonly associated with a decrease of the quality of life of patients with inflammatory bowel disease, and therefore a quick and correct diagnosis is needed, and also an adequate therapeutic approach⁽¹⁾.

Anemia is the most common systemic complication in patients diagnosed with

inflammatory bowel disease, and despite this it is under-assessed and underestimated⁽²⁾. Most of the times anemia associated with transit disorders of organic cause is a combination between iron-deficiency anemia (chronic intestinal bleeding, decreased iron absorption in the duodenum, iron-poor diet) and anemia from chronic diseases (anemia from inflammation, immunologically mediated and occurring because iron mobilization/homeostasis and erythropoietin production are influenced by cytokines and hepcidin)⁽³⁾. Unknown and untreated, anemia may adversely affect both the evolution of the subjacent disease and the patient quality of life.

According to the World Health Organization we define anemia as a hemoglobin lower than 13 g/dL in men and lower than 12 g/dL in women. Depending on the hemoglobin level anemia is classified in three grades: mild (Hb 10-12g/dL), moderate (Hb 7-10 g/dL), and severe (Hb<7g/dL).

Purpose of the study

The main objective of this study is to detect the decrease of the hemoglobin level, the character of the anemia, and also to assess the other blood cells in order to correlate the inflammation level - both systemic and intestinal - at the time of diagnosis of a patient who has transit disorders such as

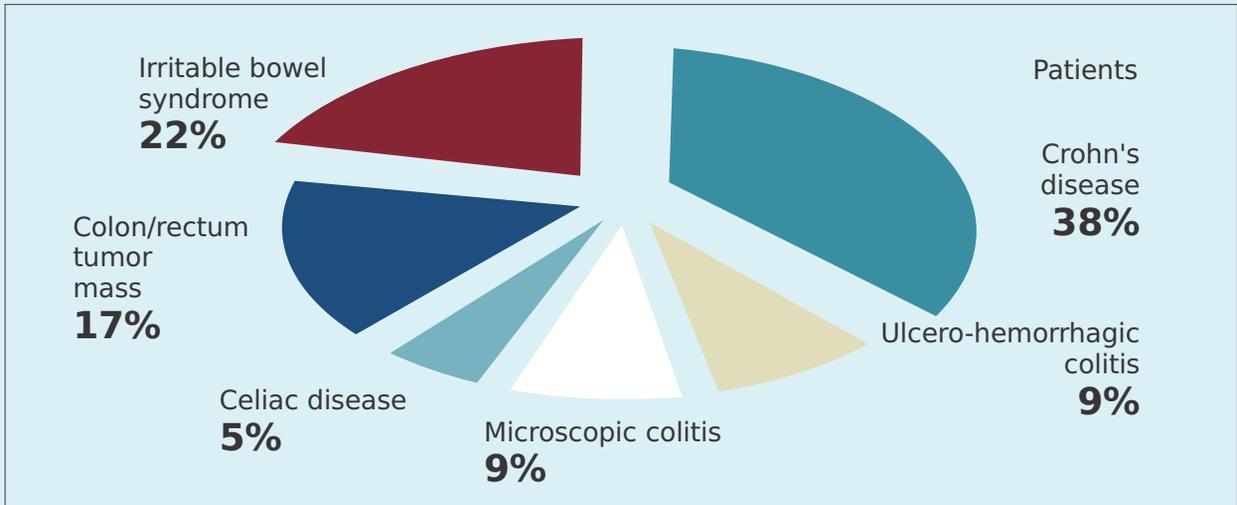


Figure 1. Representation of pathologies diagnosed following inflammations

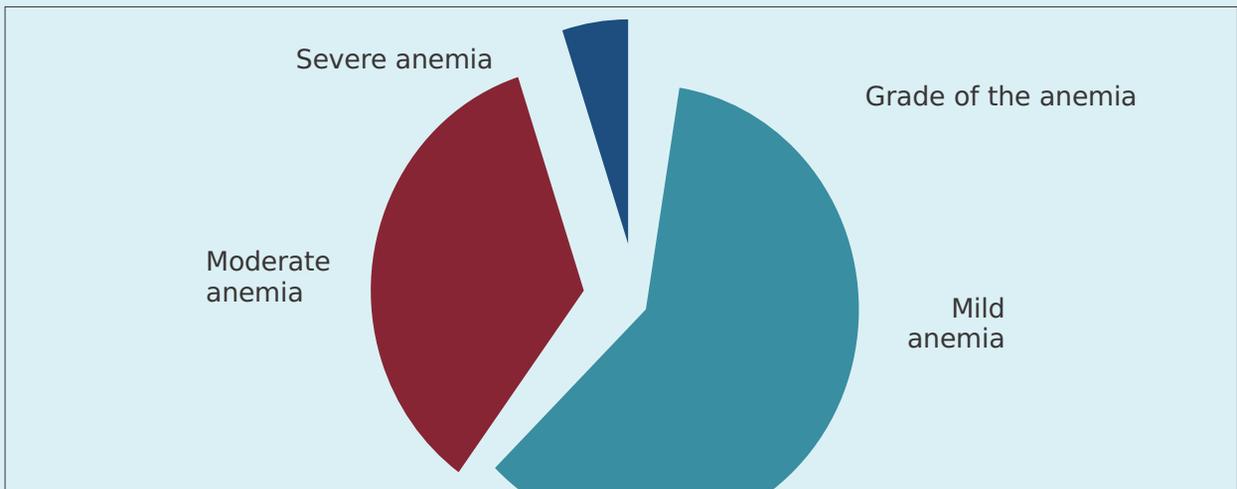


Figure 2. Distribution of anemia by hemoglobin value

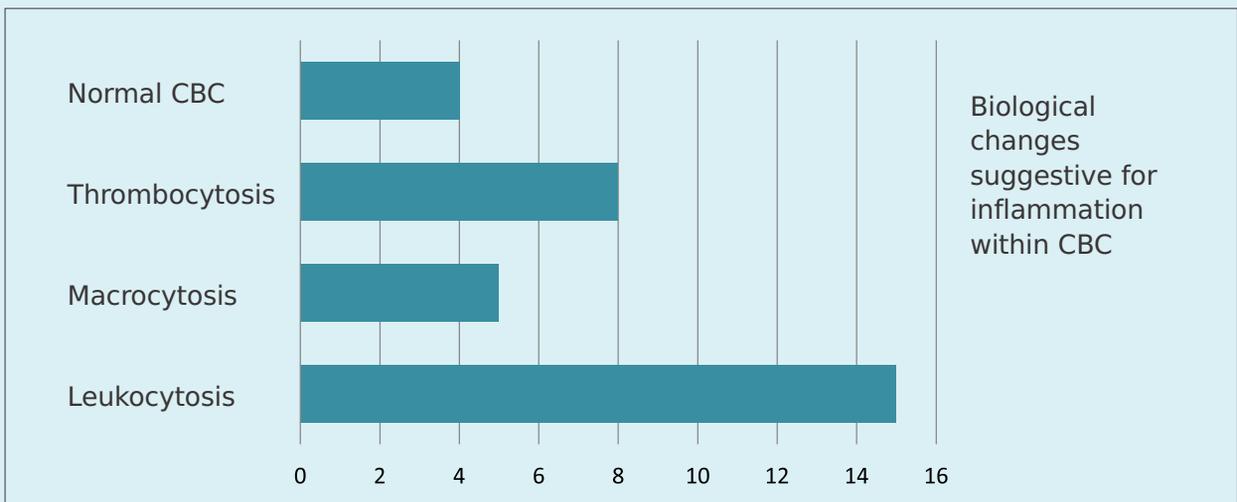


Figure 3. Assessment of blood cells suggestive for inflammation in patients with Crohn's disease



INTERNAL MEDICINE

Original papers

diarrhea or alternating diarrhea/constipation with a duration of minimum four weeks.

Material and method

A number of 81 patients were included in the study, who came to the Department Medical I of the Emergency County Clinical Hospital, Constanta, in the time period October 2014 - October 2017, and met the requested criteria, i.e. they had transit disorders such as diarrhea or alternating diarrhea/constipation with a duration of minimum four weeks. By gender distribution it was noted that 52% were women, and 48% were men. The investigations that were used included biological samples from blood (complete blood count, inflammatory syndrome represented by C reactive protein, erythrocyte sedimentation rate, fibrinogen, serum protein) and from feces (fecal cytology, stool ova and parasites exam, stool culture, calprotectin), and endoscopic assessment, i.e. upper digestive endoscopy, and colonoscopy with terminal ileoscopy (with biopsy as needed).

Results and discussions

Of the 81 included patients, 38 met the WHO criteria for anemia.

A number of 31 patients were diagnosed with Crohn's disease, 7 patients with ulcero-

hemorrhagic colitis, 7 patients with microscopic colitis, 4 patients with celiac disease, 14 patients with colorectal tumors, and 18 patients with irritable bowel. (Fig.1)

Of the patients with Crohn's disease, 15 were men with age between 22 and 72 years, with an average age of 37.6 years, and 16 were women with age between 21 and 76 years, with an average age of 46.8 years.

Based on the location of Crohn's disease, 11 patients were diagnosed with colonic location, 11 patients with Crohn's disease in the ileum and the colon, 7 cases of ileal location, 1 patient with jejunal location, and 1 case of Crohn's disease in the jejunum and the ileum.

Based on hemoglobin values 20 anemias in various forms were identified, 11 patients had hemoglobin within normal limits, with an incidence of anemia of 64.5%. We noticed a distribution by gender that was unequal, with more cases of anemia encountered in women, i.e. 12, compared to men, 8 cases.

Of the 20 cases of anemia, 8 were normochromic normocytic, 11 were hypochromic microcytic, and one macrocytic. (Fig.2)

Besides the hemoglobin value and the parameters that determine the anemia type, blood cells suggestive for inflammation were also assessed (white blood cells, monocytes, platelets). (Fig.3)

The inflammatory status was assessed from

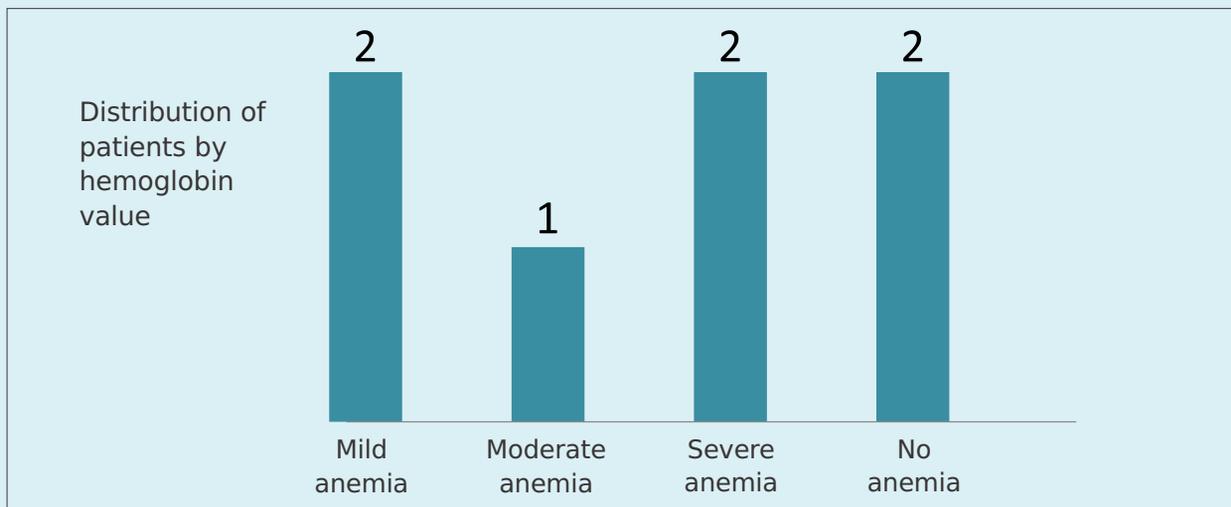


Figure 4. Distribution of patients with changes of ulcerative colitis by the grade of anemia

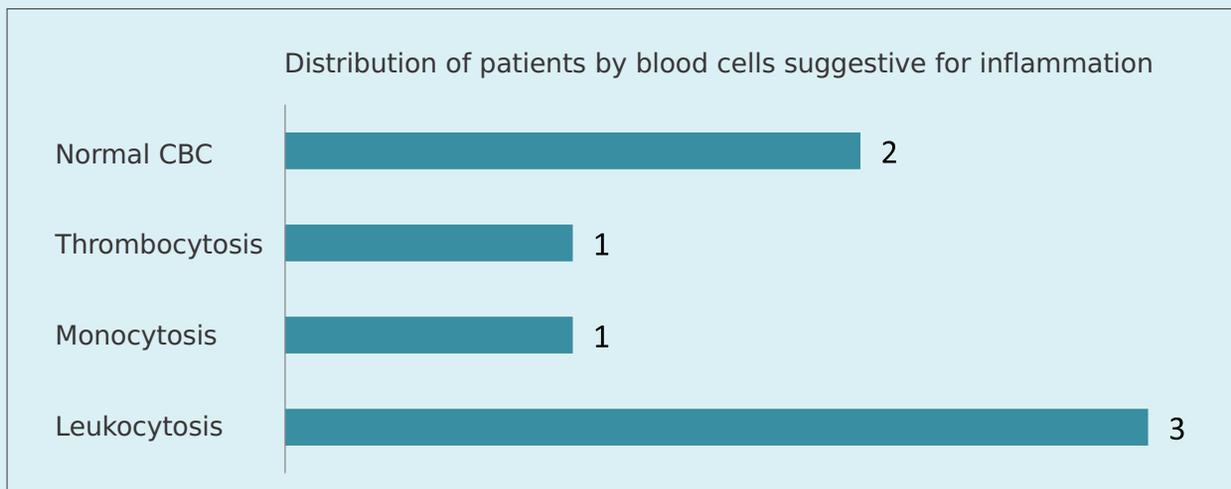


Figure 5. Distribution of patients with ulcerative colitis by blood cells

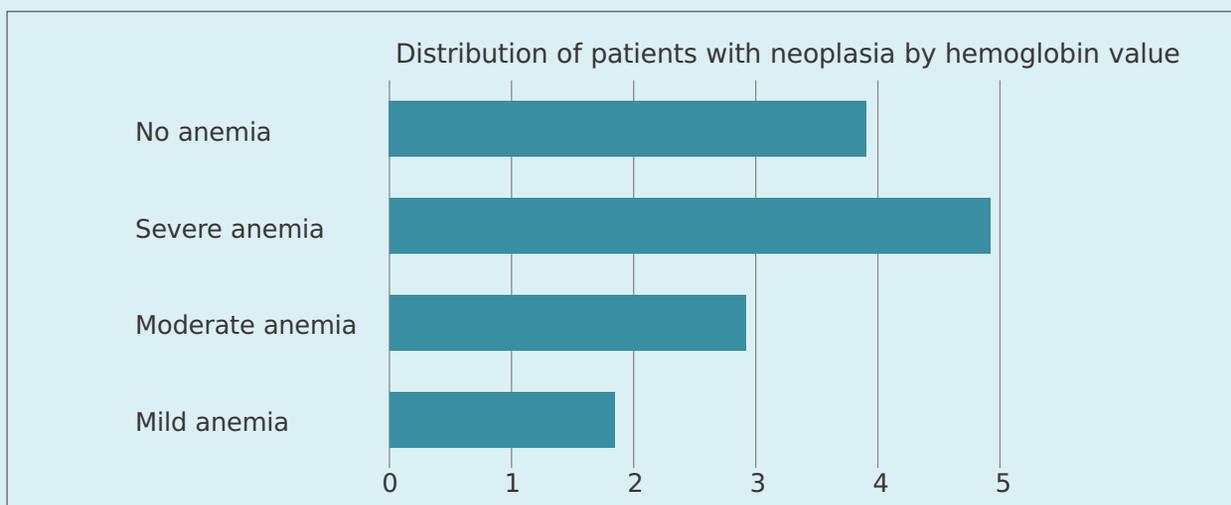


Figure 6. Distribution of patients with colon/rectum tumor mass by hemoglobin



INTERNAL MEDICINE

Original papers

the point of view of systemic inflammation (increased ESR, increased C reactive protein, increased fibrinogen) in patients with anemia and it was noticed that 15 patients of the 20 patients with anemia, i.e. 75%, had increases of all three parameters, 4 patients (205) had increase of only one inflammatory item, and 1 patient did not have inflammatory syndrome. Patients with anemia and all 3 items with increased values were checked regarding changes of blood cells, and thus 2 patients had only leukocytosis, 2 patients had leukocytosis and monocytosis, 4 patients had leukocytosis and thrombocytosis, 2 patients had leukocytosis, monocytosis, and thrombocytosis. Of the 15 patients only 5 had no change of blood cells, i.e. 33.3%.

In case of patients without anemia 6 of them had the increase of all three items responsible of systemic inflammation, 1 patient had the increase of only one item, and 4 patients had ESR, CRP and fibrinogen unchanged. Of the 6 patients with anemia and inflammatory syndrome sustained by the increase of the 3 items, 2 patients did not have any change of the complete blood count, 2 had leukocytosis, 1 patient had leukocytosis and thrombocytosis, and 1 patient had leukocytosis and monocytosis.

From these assessment we can conclude that most patients with Crohn's disease who have anemia in various grades also have markers of systemic inflammation that are present, and

this inflammation is sustained by the increase of white blood cells, and in some cases also by the increased values of platelets and monocytes. It is of note that systemic inflammation is present and well represented even in the absence of anemia.

Regarding the local inflammation assessed by fecal calprotectin, this is not correlated with the anemia grade, i.e. patients with mildly decreased hemoglobin values or even without anemia had extremely increased values of calprotectin. Of the total of patients 7 patients were diagnosed with intestinal inflammatory pathology compatible with ulcerohemorrhagic colitis, of whom 2 men with an average age of 62.5 years and 5 women with ages between 16 and 78 years, with an average age of 39 years. Based on the location of lesions 2 cases of ulcerative pancolitis were identified, 4 cases of ulcerohemorrhagic rectocolitis, and 1 case of proctitis.

Analysing the hemoglobin value we concluded that a percentage of 71.4% of patients had anemia (Fig.4). We made a comparison between the percentage of anemias from Crohn's disease (64.5%) and the percentage of anemias from ulcerative colitis (71.4%) and we concluded that there is a higher incidence of anemia in the latter. Of the total of 5 anemias 4 anemias were normochromic normocytic, and 1 was hypochromic microcytic anemia. Based on the systemic inflammation quantified by ESR, C reactive

protein and fibrinogen, followed in anemic patients, we noted in 3 patients the increase of all 3 parameters (60%), 1 patient had an increase of 2 parameters, and 1 patient had only one value increased.

All 5 patients with anemia had a very high value of calprotectin, proving that anemia was correlated with local inflammation. In case of systemic inflammation only patients with moderate and severe anemia had increases of the three parameters: ESR, C reactive protein and fibrinogen, and also increases of blood cells: white blood cells, monocytes, platelets (Fig.5).

A number of 7 patients were diagnosed with microscopic colitis, 4 men with age between 42 and 78 years, with an average age of 58.7 years, and 3 women with age between 28 and 62 years, with an average age of 43.3 years. The hemoglobin level was analyzed and we noticed that 2 patients had mild hypochromic microcytic anemia, with an incidence of anemia of 28.5%, and 5 patients had a complete blood count without pathological items. All patients had increased calprotectin value, between 91 mg/kg and 474 mg/kg, an no notable differences were identified between patients who had anemia and those with unchanged hemoglobin.

Of the 5 patients without anemia, 4 did not have systemic inflammatory syndrome (ESR with normal value, normal CRP, without change of blood cells), and one patient had a discrete increase of two components that showed systemic inflammation (ESR, fibrinogen). We can conclude that the absence of anemia is correlated with the absence of systemic inflammation, but not with the absence of local intestinal inflammation.

Although celiac disease does not have at its basis an inflammatory mechanism, as it is an immune system condition, triggered by the intake of dietary gluten, in which small bowel

injuries occur, it was included in the study because the patients diagnosed with this pathology met the acceptability criteria.

A number of 4 patients were diagnosed with celiac disease, one woman and 3 men with age between 19 and 60 years, with an average age of 32.6 years.

Of the 4 patients, one had moderate hypochromic microcytic anemia, and the other 3 had hemoglobin with normal value. The patient with anemia did not have inflammatory syndrome, while of the 3 patients without anemia 2 have no inflammatory syndrome, one had leukocytosis and discreetly increased C reactive protein.

A number of 14 patients were diagnosed with colorectal masses, with an equal gender distribution, 7 men with age between 55 and 68 years, with an average age of 59.8 years, and 7 women with age between 53 and 89 years, with an average age of 74.2 years.

Of the 10 cases of anemia 8 were hypochromic microcytic and 2 were normochromic normocytic (Fig. 6).

Analysing the parameters responsible for systemic inflammation in patients who had various grades of anemia it is noted that 3 patients had all 3 parameters increased, 3 patients had 2 parameters increased, 3 patients had one parameter increased, and one patient did not have inflammatory syndrome.

In case of patients with colorectal neoplastic masses the tumor marker was analyzed, i.e. the carcinoembryonic antigen (CEA). Of the 4 patients with normal hemoglobin 3 patients had ACE with increased value, i.e. 75%, and of the 10 patients with anemia only 4 had increased ACE, i.e. 40%. From these data we can conclude that the presence of the anemia is not correlated with an increased value of the tumor marker. It is known that the plasma concentration of the marker is quite poorly



INTERNAL MEDICINE

Original papers

correlated with the tumor mass. A number of 18 patients were diagnosed with irritable bowel syndrome, 8 men with age between 28 and 60 years, with an average age of 38.3 years, and 10 women with age between 37 and 70 years, with an average age of 64.2 years. No patient had anemia. Regarding the inflammatory syndrome 14 patients had all parameters within normal limits, 1 patient had one parameter increased, 1 patient had two parameters increased, and 1 patient had all 3 parameters with increased value. Analysing the local inflammation quantified by the value of fecal calprotectin it was noted that 13 patients had calprotectin within normal limits, while 2 patients had a discreetly increased value. From the obtained data it is certified that in irritable bowel there are no changes of an organic nature, only a functional issue. However research on intestinal microbiota are starting to contradict the idea that the irritable bowel syndrome is an exclusively functional disorder⁽⁴⁾.

Anemia is the most common complication of inflammatory bowel diseases, although for a long time it was not a diagnostic priority for clinicians⁽⁵⁾.

Conclusions

In case of patients diagnosed with Crohn's disease 64.5% had anemia, and 75% of the patients with anemia and Crohn's disease had

inflammatory syndrome. Local inflammation is not correlated with the grade of anemia in patients with Crohn's disease, as the incidence of anemia is higher in patients with ulcerative colitis compared with patients diagnosed with Crohn's disease (71.4% vs 64.5%). Local inflammation is correlated with the presence of anemia in case of patients with ulcerative colitis, while systemic inflammation is correlated only with the presence of moderate and severe anemia. In case of patients diagnosed with microscopic colitis the absence of anemia is correlated with the absence of systemic inflammation, but not with the absence of local inflammation.

References

1. Escott G., Rosso R., Oliveira Neto PA de, Peres A. Prevalence of anemia in inflammatory bowel disease. *Ciência em Movimento* 2009; 11: 75-80. 353.
2. Rothfuss KS, Stange EF, Herlinger KR. *Extraintestinal manifestations and complications in inflammatory bowel diseases*. *World J Gastroenterol* 2006;12:4819-31
3. Cijevschi Prelipcean Cristina, Mihaela Dranga, Gabriela Ștefănescu, Cătălina Mihai Valențele fierului în boala inflamatorie intestinală. In Stanciu C (redactor). *Actualități în Gastroenterologie și Hepatologie*. Editura Junimea, Iași. 2010: 124-139
4. Sood R, Ford AC. *Use of biomarkers in irritable bowel syndrome: to predict the future, look at the past*. *Clin Transl Gastroenterol*. 2015
5. Cijevschi Prelipcean Cristina, Mihaela Dranga, Gabriela Ștefănescu, Cătălina Mihai Valențele fierului în boala inflamatorie intestinală. *Actualități în Gastroenterologie și Hepatologie*. Editura Junimea, Iași. 2010:124-139.