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Research Article

The Role of Anemia of Inflammation in the Course of Chronic HBV Infection in Children

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Abstract

The article evaluates the features of the course of chronic HBV infection in children with the background of anemia of inflammation. A brief description of the clinical and laboratory manifestations of the disease is given, depending on the course of anemia and inflammation. The data on hepcidin dynamics are analyzed. The stage–by-stage formation of iron metabolism disorders was revealed, in the form of a true deficiency with a breakdown of ferrokinetic markers – an increase in hepcidin and soluble transferin receptors with the background reduced ferritin values characteristic of iron deficiency anemia in the initial stages of the disease and, redistributive iron deficiency - decrease in hepcidin and soluble transferrin receptors with the background increased ferritin values characteristic of iron overload the body is in the late stages of the disease.

Introduction

Despite large-scale vaccination against hepatitis B, to date, the problem of chronic HBV infection remains one of the most pressing health issues, maintaining high medical and social importance throughout the world [1-3]. At the same time, various conditions act as modifying factors for the progression of the pathological process in the liver, which, proceeding from the perspective of concomitant diseases, cause the development of two or more mutually reinforcing processes. There is a high probability of developing anemia of inflammation (up to 95%) in cases of chronic HBV infection in children and insufficient attention to its treatment (80%) due to several medical and social reasons, such as complete disregard (30%), the development of refractory treatment with iron preparations (40%), frequent relapses (98.6%) late diagnosis (up to 45%), etc., have formed the problem of combined pathology, which requires its solution [4,5]. There is a close physiological relationship between pathogenetic aspects, in particular, on the one hand, the pathological process in liver (decreased absorption of iron in intestine as a result of viral persistence in enterocytes, liver involvement in the synthesis of proteins transporting and depositing iron, the development of occult hemolysis of erythrocytes, disorders of iron reutilization and erythropoiesis, etc.); on the other hand, the anemic process (hemic and tissue hypoxia, disorders of the LPO/AOS system and intracellular metabolism, formation of membranopathies, regenerative plastic dysfunction syndrome, etc.), initiated by viral replication, contribute to the suppression of the general resistance of the macroorganism and makes all the ways of progression of chronic HBV infection real [6-9]. In addition, if we consider that it is hepatocytes that synthesize the hormone–like protein hepcidin, a universal regulator of iron metabolism that affects both intestinal absorption of dietary iron and the release of iron from macrophages during recirculation from red blood cells [10,11], then it can be argued that liver plays a significant role in the genesis of hemosideric state. The expression of hepcidin leads to iron deficiency, while a decrease leads to hemosiderosis. The gene that triggers the intracellular mechanism of hepcidin transcription is expressed by inflammatory mediators and elevated iron levels in the blood, and is inhibited by hypoxia

and activation of hematopoiesis [12,13]. At the same time, the level of hepcidin can vary from a sharp increase to minimally low values, depending on the activity of regulatory proteins that ambiguously respond to inflammation [14-16]. Thus, the high probability of developing anemia of inflammation in children with chronic HBV infection forced us to take a closer look at the problem of combined pathology. In this regard, the study aimed to evaluate the features of the course of chronic HBV infection in children, depending on the different variants of the course of anemia of inflammation.

Materials and methods

A total of 140 children with chronic HBV infection aged 7 to 18 years were examined. The fact of anemia was established according to WHO criteria - the concentration of hemoglobin (Hb) in capillary blood in children over 12 years old < 120 g/l, 5 - 12 years old < 115 g/l, and under 5 < 110 g/l. All children underwent a comprehensive examination, including complaints, anamnesis of life and illness, and a clinical examination. Inclusion criteria: children with chronic HBV infection and low hemoglobin levels. Exclusion criteria were children with chronic HCV and HDV infection, vitamin B12 and folate deficiency anemia. A common blood test was performed on a hematological automatic analyzer "Mindray" model VS-5800 (China). The levels of soluble transferrin receptors (sTfR) and ferritin (Ft) were studied by ELISA using (Accu-Bind, USA). Virological verification was performed based on the detection of HBsAd, HBsAb, HBeAd, HBeAb, HBcorAb by ELISA using Human kits (Germany). A PCR study for the qualitative and quantitative determination of HBV DNA was performed with real-time hybridization-fluorescence detection on a BIO-RAD iQ5 amplifier (USA) using HBV-FL, HCV-FL, and HDV-FL amplification kits (Russia). Biochemical blood testing was performed using standardized methods using commercial ROCHE kits on a Cobas® 6000 core biochemical analyzer. The determination of fibrinogen content, prothrombin time (PTT), and activated partial thromboplastin time (APTT) was performed on a Human Huma Clot Duo Plus device using kits NHF, HHT-SI, and HNA-EL (Germany). Protein fractions were determined by means of electrophoresis on an acetate cellulose film using HUMAN kits (Germany). Special research methods included ELISA determination of the biologically active form of peptide hepcidin-25 (Enzyme Immunoassay, USA) and pro-inflammatory cytokines (IL-1, IL-6) – (eBioscience, Austria). The control group consisted of 30 practically healthy children. Ultrasound examination of liver, spleen, and biliary tract with Dopplerography of portal system vessels was performed on a Philips ClearVue 650 device (USA), as well as elastometry of liver tissue with a total density calculation in kPa. Statistical data processing was carried out using the variational statistics method using Excel 2007 Statistica 6.0 software and the Student's t-test.

Results and discussion

It was interesting to determine the informative value of various ferrokinetic markers that are directly involved in iron metabolism in the diagnosis of anemia of inflammation in children with chronic HBV infection. It is known that the serum ferritin level reflects the amount of iron deposited, while the sTfR level reflects the degree of iron availability to cells. Ferritin is the "acute phase protein" of inflammation, which correlates with markers of cell damage, markers of hydroxyl radical formation, and the severity of the disease. In particular, in our studies, its values ranged widely from 10.8 ng/ml to 152.3 ng/ml, which makes it difficult to interpret the significance of this marker. Unlike ferritin, sTfR is not involved in "acute phase reactions"; its level does not depend on the presence of inflammation or infection. Analysis of research papers has shown that the concentration of sTfR and ferritin for calculating the $sTfR/\log_{10}Ft$ index increases the diagnostic accuracy (sensitivity 81%, specificity 83%) of iron metabolism disorders in patients with chronic diseases [17,18]. The calculation of the index showed that its maximum values were in the range of 2,864, and the minimum values were 0.635, with a control of 1.45 ± 0.30, $p > 0.05$. According to the authors [19], index values >2 indicate depletion of iron reserves in the body, i.e., "true" iron deficiency; in contrast, <1 indicates redistributive iron deficiency, indicating an overload of iron in the body. Depending on the index values, the sick children were divided into 2 groups: 60.7% of children with index values of $sTfR/\log_{10}Ft<1$ (0.994 ± 0.01) were in the I group, while the other 39.3% of children with index values of $sTfR/\log_{10}Ft>2$ (2.237 ± 0.18) were in the II group. In the I-group of the patients, there turned out to be 57.8% of the children with severe and 42.2% with moderate disease activity. The absence of minimal activity of chronic HBV infection in this group was noted, while the duration of the disease was 10.4 ± 0.29 years. Group II included 72.4% of children with minimal and 27.6% with moderate activity, where the duration of the disease was 3.04 ± 0.12 years. The study of the role of anemia of inflammation in the formation of the clinical course of chronic HBV infection in children showed that, with the background predisposing deficiency, the disease was much more severe, prolonging the period of clinical exacerbation and the prevalence of pronounced (72.9%) and progressive (49.4%) forms of the disease, which generally characterized the status of prolonged chronic stress. The clinical course of chronic HBV infection with the background anemia of inflammation in children was characterized by a persistent predominance of all clinical syndromes ($p < 0.01$). At the same time, intragroup analysis revealed the prevalence of such syndromes as asthenovegetative (95.3%), hemorrhagic (90.6%), hepatomegaly (100%), and splenomegaly (77.6%) in the I group of children. The study of the symptoms characteristic of the anemic process allowed us to identify such complaints as tinnitus and palpitations, which were more often presented by children of group I (68.2 ± 5.0% and 64.7 ± 5.2% *vs.* 40.0 ± 6.0% and 43.6 ± 6.7% $p < 0.05$). During the examination, such manifestations as brittle nails (89.4 ± 3.3% *vs.* 54.5 ± 6.7%), deformity of the nail plates (54.1 ±

5.4% *vs.* 30.9 ± 6.2%), dryness and abundant hair loss (77.6 ± 4.5% *vs.* 52.7 ± 6.7%) cracks on the finger pads attracted our attention (29.4 ± 4.9% *vs.* 12.7 ± 4.5%, respectively, groups I and II, $p < 0.001$ - 0.05). Abnormal changes in taste (pica chlorotica) were also more often detected in the I group of children in the form of picacism – eating clay, chalk, earth, raw dough (2 times), pagophagia – eating frozen foods and ice (4.7 times), pathosmia – addiction to unpleasant odors like sniffing varnish, paints, acetone, etc . (1.8 times) and a tendency to develop stomatitis (1.8 times, $p < 0.05$). The next stage was the study of the HBV marker profile in sick children, depending on the values of the sTfR/$\log_{10}$Ft index. According to the data (Table 1), the prevalence of a marker indicating high infection, HBeAd ($p < 0.05$), was detected in the patients of group I. Along with this, marker of active replication HBV–DNA was found in all children of this group with copy number variations in the range of 106-108copies/ml. In children of group II, this marker was found in 75% of the cases with variations in the number of copies in the range of 104 - 105 copies/ml ($p < 0.01$).

Thus, the patients with redistributive iron deficiency were characterized by pronounced viral aggression with a high viral load, which predetermined the severity of the disease.

Comparative analysis of laboratory test results confirmed a more severe status in group I children (Table 2), where the leading indicators of functional liver damage were the syndromes of endotoxemia (95.3%), mesenchymal inflammation (92.9%), and cytolysis with the development of prolonged hyperfermentemia (82.4%).

Table 1: Prevalence of HBV markers depends on the values of sTfR/$\log_{10}$Ft index, %.

	sTfR/$\log_{10}$Ft<1 index	sTfR/$\log_{10}$Ft>2 index
HBsAg	100.0	100.0
HBsAb	0.0 ± 0.0*	15.6 ± 6.4
HBeAg	92.8 ± 4.9*	71.8 ± 7.9
HBeAb	7.1 ± 4.9*	31.2 ± 8.2
HBcorAb	82.1 ± 7.4	78.1 ± 7.3
HBV-DNA	100.0*	75.0 ± 11.2

N.B. * - Reliability of the difference between the examined groups.

Table 2: Laboratory data in children with chronic HBV infection depend on the values of sTfR/$\log_{10}$Ft index.

	sTfR/$\log_{10}$Ft<1 index	sTfR/$\log_{10}$Ft>2 index	Control
ALT, U/L	124.9 ± 8.5*,**	78.0 ± 2.3	37.0 ± 3.8
AST, U/L	82.1 ± 4.8*,**	59.1 ± 1.7	25.0 ± 2.5
Total bilirubin, µmol/l	48.4 ± 3.0*,**	31.6 ± 1.6*	14.8 ± 1.5
Gamma GT	84.0 ± 2.5*,**	38.4 ± 1.2*	33.3 ± 3.4
Alkaline phosphatase, U/L	405.6 ± 17.1*,**	320.8 ± 12.9*	177.0 ± 18.2
Gamma globulin, %	31.9 ± 0.52*,**	26.1 ± 0.32*	15.7 ± 1.6
Albumin, %	39.6 ± 0.64*	44.4 ± 0.8*	54.5 ± 5.6
Fibrinogen, g/l	1.87 ± 0.04*,**	1.96 ± 0.04*	3.93 ± 0.14
Prothrombin time, seconds	23.7 ± 0.53*,**	21.7 ± 0.27*	16.5 ± 1.7
APTT, seconds.	36.5 ± 0.31*a	25.8 ± 0.21	24.4 ± 0.72

N.B. difference reliability * - To control group; ** - between I and II groups ($p < 0.05$-0.001).

Thus, the results of a comparative analysis of the clinical course showed that the development of anemia of inflammation causes prolongation of the clinical and biochemical syndromes of the disease and HBV viral activity. Apparently, one of the reasons for the progression of both the pathological process in the liver and HBV activity is the presence of an anemic process that initiates and exacerbates a cascade of pathophysiological processes. The obtained data clearly emphasized the importance of timely diagnosis of anemia of inflammation in chronic HBV infection in children.

In the study of common blood test (Table 3), a decrease in erythrocytes and hemoglobin was detected in both groups; however, analysis of erythrocyte hemogram indices revealed differences in the morphological characteristics of erythrocytes and the degree of hemoglobin saturation of erythrocytes ($p < 0.001$).

Thus, the indicators of common blood test for children with chronic HBV infection with the background true iron deficiency had distinguished descriptive value by microcytic 76.4 ± 5.7%, hypochromic 85.5 ± 4.7% anemia with heterogeneous anisocytosis 63.6 ± 6.4% ($p < 0.001$). In contrast, normocytic 65.9 ± 5.1% normochromic 67.1 ± 5.0% anemia, 53% leukopenia with an average value (3.88 ± 0.14 × 109/l), and 82.7% thrombocytopenia with an average value (107.460 ± 4.05 × 109/l) were characteristic of the children with predisposing deficiency. It can be stated that the combination of low hemoglobin levels with abnormalities in erythrocyte hemogram indices may indicate a predisposing iron deficiency, which is a criterion for iron overload syndrome in chronic HBV infection in children.

It is known that hepcidin is synthesized in hepatocytes in the form of a prepropeptide of 84 amino acids, is excreted into the circulation in the form of a mature, structured peptide of 25 amino acids, and is one of the main humoral regulators of iron metabolism in the body. The level of hepcidin can vary from a sharp increase to minimally low values, depending on the activity of regulatory proteins that ambiguously respond to inflammation. Transcription of mRNA hepcidin in hepatocytes is induced by proinflammatory cytokines through the intracellular JAK-STAT (Janus kinase/signal transducer and activator of transcription) signaling pathway [10]. Despite the high inflammatory index in the examined patients, especially in group I children (IL-1 up to 9.81 ± 0.63 pg/ml and IL-6 up to 12.85 ± 0.50 pg/ml $p < 0.05$), the dynamics of hepcidin-25 revealed ambiguous results (Table 4). Specifically, children with chronic HBV infection with anemia of inflammation were divided into 2 categories - 69.5% of children with low (28.68 ± 0.6 ng/ml) and 30.5% with high (56.37 ± 1.6 ng/ml) levels of hepcidin–25 (control 39.4 ± 1.7 ng/ml), which corresponded in the first case to the vast majority (91.7%) of group I patients, in the second, the majority (81.9%) of group II children. At the same time, it was noted that in the I group of patients, more than half (57.8%) of the children had pronounced activity of

Table 3: Haemogram data in children with chronic HBV infection depend on the values of sTfR/log_{10}Ft index.

	sTfR/log_{10}Ft<1 index	sTfR/log_{10}Ft>2 index	Control
RBC × 10^{12}/l	3.9 ± 0.05*	3.8 ± 0.06*	4.62 ± 0.07
Hb, g/l	102.9 ± 0.6*,**	95.9 ± 0.8*	124.1 ± 0.85
MCV, fl microcytic normocytic	82.5 ± 0.55** 75.4 ± 0.4* (34.1%) 86.2 ± 0.43 (65.9%)	78.4 ± 0.74* 75.9 ± 0.4* (76.4%) 85.6 ± 1.0 (23.6%)	86.2 ± 0.67
MCH, pg hypochromic normochromic	30.0 ± 0.2** 25.5 ± 0.31*(32.9%) 30.4 ± 0.05 (67.1%)	25.7 ± 0.30* 24.9 ± 0.21*(85.5%) 30.4 ± 0.3 (14.5%)	32.5 ± 1.77
MCHC, g/l	319.0 ± 1.5*	318.4 ± 1.7*	340.0 ± 2.51
RDW, % homogeneous heterogeneous	13.8 ± 0.15** 13.0 ± 0.08 (76.5%) 16.3 ± 0.2*** (23.5%)	4.8 ± 0.17* 13.4 ± 0.1(36.4%) 15.7 ± 0.1*(63.6%)	13.0 ± 0.89 (100%)
WBC × 10^9/l	3.88 ± 0.14*,**	6.13 ± 0.19*	7.02 ± 0.16
PLT ×10^9/l	107.460 ± 4.05*,**	250.000 ± 3.1*	270.100 ± 6.2
MPV, mm^3	9.0 ± 0.08*,**	8.4 ± 0.06	8.3 ± 0.15
PDW, %	17.2 ± 0.07*,**	16.2 ± 0.08	15.97 ± 0.08
PCT, %	0.10 ± 0.01*,**	0.19 ± 0.0*	0.21 ± 0.01

N.B. difference reliability * - to control group; ** - between I and II groups (p < 0.05 - 0.001).

Table 4: Markers of inflammation depend on the values of sTfR/log_{10}Ft index in children with chronic HBV infection.

	sTfR/log_{10}Ft<1 index	sTfR/log_{10}Ft>2 index	Control
Hepcidin-25, ng/ml	28.68 ± 0.6*,**	56.37 ± 1.6*	39.4 ± 6.5
IL-1, pg/ml	9.81 ± 0.63*,**	8.22 ± 0.45*	6.45 ± 0.34
IL-6, pg/ml	12.85 ± 0.50*,**	9.20 ± 0.43	7.75 ± 0.75

N.B. difference reliability * - to control group; ** - between I and II groups (p < 0.05 - 0.001).

chronic HBV infection, whereas in the II group, the majority of children (72.4%) had minimal activity of the disease.

In our opinion, in cases of true iron deficiency, this is due to the preservation of hepatocytes and is considered an acceptable process in the form of a response of increased synthesis of hepcidin-25 to an inflammatory stimulus. In cases of redistributive deficiency, despite the high inflammatory index, decrease in hepcidin-25 levels is associated with increased mesenchymal inflammatory processes in liver, accumulation of free radicals, which generally leads to the failure of receptor structures on hepatocyte membranes with the development of a block of the intracellular regulatory system for the synthesis of this peptide, decrease in the compensatory capabilities of the body and progression of the disease. This was also confirmed by studying the level of hepcidin-25 depending on the stage of the disease. Thus, the highest average values of this indicator were found among children with chronic HBV infection with a disease duration of up to 3 years (62.90 ± 4.8 ng/ml). With a disease duration of 3 to 5 years, the average values of hepcidin-25 decreased to 28.12 ± 1.3 ng/ml. At the same time, the lowest values were found with a duration of chronic HBV infection over 5 years, where the average values of the indicator were reduced to 16.47 ± 0.6 ng/ml (p < 0.001, between the compared groups). Thus, in cases of chronic HBV infection in children, the increased level of hepcidin-25 in the early periods of the disease tended to decrease as the pathological process in the liver and the duration of the disease increased. Pathogenetically, these changes reflected virus-induced pathological stress reactions, during which, as a result of various metabolic shifts, damaging mechanisms are formed and, already in conditions of a combined course, contribute to the development of two parallel mutually reinforcing processes that cause the progressive course of chronic HBV infection.

Conclusion

In cases of chronic HBV infection in children, in the genesis of anemia of inflammation, a stage–by-stage formation of changes has been established, in the form of a true iron deficiency with a breakdown of ferrokinetic markers - increase in hepcidin and indicators of soluble transferrin receptors with the background reduced ferritin values characteristic of iron deficiency anemia in the initial stages of the disease and redistributive iron deficiency (lack of “active” forms of iron on the background of the growth and deposition of siderophyllins) – decreased hepcidin and indicators of soluble transferrin receptors with the background increased ferritin values, characteristic of hemosiderosis in the late stages of the disease. In conditions of redistributive iron deficiency, chronic HBV infection was much more severe, as evidenced by the prevalence of more pronounced (72.9%) and progressive (49.4%) forms of the disease with pronounced viral aggression and high viral load (100%). To detect iron deficiency of “true” or cumulative origin, additional ferrokinetic monitoring using diagnostic markers (sTfR/log_{10}Ft index with the level of hepcidin-25) is necessary. Timely differential diagnosis of variants of the course of anemia of inflammation makes it possible to exclude unjustified administration of iron preparations and help reduce the development of progressive forms of chronic HBV infection in children.

Conflict of interest statement

The article is published for the first time and is part of a scientific work.

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Ethical approval and consent to participate

The Research Ethics Board of our institution does not require review or approval of case reports. Our research was carried out in accordance with the World Medical Association Code of Ethics (Declaration of Helsinki).

References

1. World Health Organization. Global hepatitis report; 2024. Available from: https://www.who.int/publications/b/76480
2. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of chronic hepatitis B virus infection. J Hepatol. 2017;67(2):370–398. Available from: https://www.journal-of-hepatology.eu/article/S0168-8278(17)30185-X/fulltext
3. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis—2020 update. J Hepatol. 2021;75(3):659–689. Available from: https://www.journal-of-hepatology.eu/article/S0168-8278(21)00398-6/fulltext
4. Toima S, Saleh A, Madkour M. Role of hepcidin in anemia of chronic hepatitis C patients. J Am Sci. 2010;6(12):145–154. Available from: http://www.americanscience.org
5. Tsochatzis E, Papatheodoridis GV, Koliaraki V, Hadziyannis E, Kafiri G, Manesis EK, et al. Serum hepcidin levels are related to the severity of liver histological lesions in chronic hepatitis C. J Viral Hepat. 2010;17(11):800–806. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2893.2009.01244.x
6. Khadr N, Okasha H, Nouh H, Semary W. Monitoring hepcidin level in chronic hepatitis C virus patients during therapy. Afro-Egypt J Infect Endem Dis. 2014;4(4):184–194. Available from: https://aeji.journals.ekb.eg/article_17201.html
7. Camaschella C, Nai A, Silvestri L. Iron metabolism and iron disorders revisited in the hepcidin era. Haematologica. 2020;105(2):260–272. Available from: https://www.haematologica.org/article/view/9569
8. Nemeth E, Ganz T. Hepcidin-ferroportin interaction controls systemic iron homeostasis. Int J Mol Sci. 2021;22(12):6493. Available from: https://www.mdpi.com/1422-0067/22/12/6493
9. Silva B, Faustino P. An overview of the molecular basis of iron metabolism regulation and the associated pathologies. Biochim Biophys Acta. 2015;1852(7):1347–1359. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0925443915000693
10. Ganz T. Hepcidin and iron regulation, 10 years later. Blood. 2011;117(17):4425–4433. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0006497115309994
11. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood. 2019;133(1):40–50. Available from: https://ashpublications.org/blood/article/133/1/40/263619
12. Girelli D, Nemeth E, Swinkels DW. Hepcidin in the diagnosis of iron disorders. Blood. 2016;127(23):2809–2813. Available from: https://ashpublications.org/blood/article/127/23/2809/35135
13. Lee P, Peng H, Gelbart T, Wang L, Beutler E. Regulation of hepcidin transcription by interleukin-1 and interleukin-6. Proc Natl Acad Sci U S A. 2005;102(6):1906–1910. Available from: https://www.pnas.org/doi/10.1073/pnas.0409808102
14. Nemeth E, Ganz T. Hepcidin and iron-loading anemias. Haematologica. 2006;91(6):727–732. Available from: https://pubmed.ncbi.nlm.nih.gov/16769573/
15. Schwartz AJ, Das NK, Ramakrishnan SK, Jain C, Jurkovic MT, Wu J, et al. Hepatic hepcidin/intestinal HIF-2alpha axis maintains iron absorption during iron deficiency and overload. J Clin Invest. 2019;129(1):336–348. Available from: https://www.jci.org/articles/view/122359
16. Silva B, Faustino P. An overview of the molecular basis of iron metabolism regulation and the associated pathologies. Biochim Biophys Acta. 2015;1852(7):1347–1359. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0925443915000693
17. Punnonen K, Irjala K, Rajamaki A. Serum transferrin receptor and its ratio to serum ferritin in the diagnosis of iron deficiency. Blood. 1997;89(3):1052–1057. Available from: https://ashpublications.org/blood/article/89/3/1052/137404
18. Oustamanolakis P, Koutroubakis IE, Messaritakis I, Niniraki M, Kouroumalis EA. Soluble transferrin receptor-ferritin index in the evaluation of anemia in inflammatory bowel disease: a case-control study. Ann Gastroenterol. 2011;24(2):108–114. Available from: https://pubmed.ncbi.nlm.nih.gov/24713758/
19. Skikne BS, Punnonen K, Caldron PH, Bennett MT, Rehu M, Gasior GH, et al. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: a prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index. Am J Hematol. 2011;86(11):923–927. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ajh.22108