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Article

Assessment of Hemodynamic Parameters by Type of Anemia in Children with Chronic Kidney Disease

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Abstract: The article presents the diagnostic significance and comparison of hemodynamic and cytokine indicators in different types of anemia in children with chronic kidney disease. Values of iron metabolism indicators (serum iron and ferritin, transferrin), hemoregulatory hormones (erythropoietin and hepcidin), and blood inflammation markers (IL-6 and TNF-α) were identified. Functional anemia in children is more severe compared to absolute anemia. Thus, laboratory diagnostics should be conducted for all patients with chronic kidney disease, starting in the early stages of the disease.

Keywords: anemia, chronic kidney disease, anemia of chronic disease, serum iron, serum ferritin, transferrin, erythropoietin, hepcidin.

1. Introduction

Chronic kidney disease (CKD) in children is a significant medical problem with limited data on its exact prevalence [1]. The prevalence of CKD may be higher due to insufficient diagnosis and treatment of diseases leading to CKD [1-5]. The Ministry of Health of Uzbekistan researches the increasing number of children suffering from CKD. Rural areas have higher rates of the disease [6]. Anemia is a common complication of CKD in children. Scientific data has shown that hemoglobin levels depend on the level of iron in the blood [6-10]. Iron deficiency is found in 42% of CKD patients, and anemia increases with the worsening stage of CKD [5, 17, 18]. Hepcidin is an important factor for iron regulation in the body [19]. Research continues to address the diagnostic problems of anemia in children with CKD [12-14, 20-25]. CKD can also affect the functions of other organs, leading to more serious health problems [9-11, 15]. Support and adequate medical care are critical to improving the prognosis for children with CKD [16].

Study Objective: To evaluate the indicators of erythropoietin and hepcidin hormones, iron metabolism (serum iron and ferritin, transferrin), and cytokine markers in the blood to determine the predominant nature of anemia (absolute or functional) and identify their significance depending on the stage of chronic kidney disease.

2. Materials and Methods

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A study was conducted involving 95 children aged 4 to 15 years diagnosed with chronic kidney disease. The children were divided into 3 groups. Group I consisted of 25 children with anemia syndrome in stage I CKD. Group II included 51 children with anemia syndrome in stage III CKD, and Group III included 19 children with anemia syndrome in stage IV CKD. For Group IV (comparison group), 25 children with anemia syndrome without signs of renal pathology were selected. Blood was taken from the children to determine serum iron, serum ferritin, transferrin, erythropoietin, hepcidin, interleukin-6 and tumor necrosis factor-alpha.

Based on the study results, 30% (29) of children with CKD were diagnosed with absolute anemia based on normal and elevated erythropoietin levels (subgroup A). In contrast, 70% (66) of children with CKD were diagnosed with functional anemia based on low erythropoietin levels (subgroup F) (Fig. 1). Absolute anemia was found in 100% of children in Group IV (comparison group) (Fig.1).

3. Results

A comprehensive blood test revealed varying degrees of anemia in 100% of children. Anemia was moderate in 90% (86) of cases, mild in 4% (4) of cases, and severe in 5% (5) of cases.

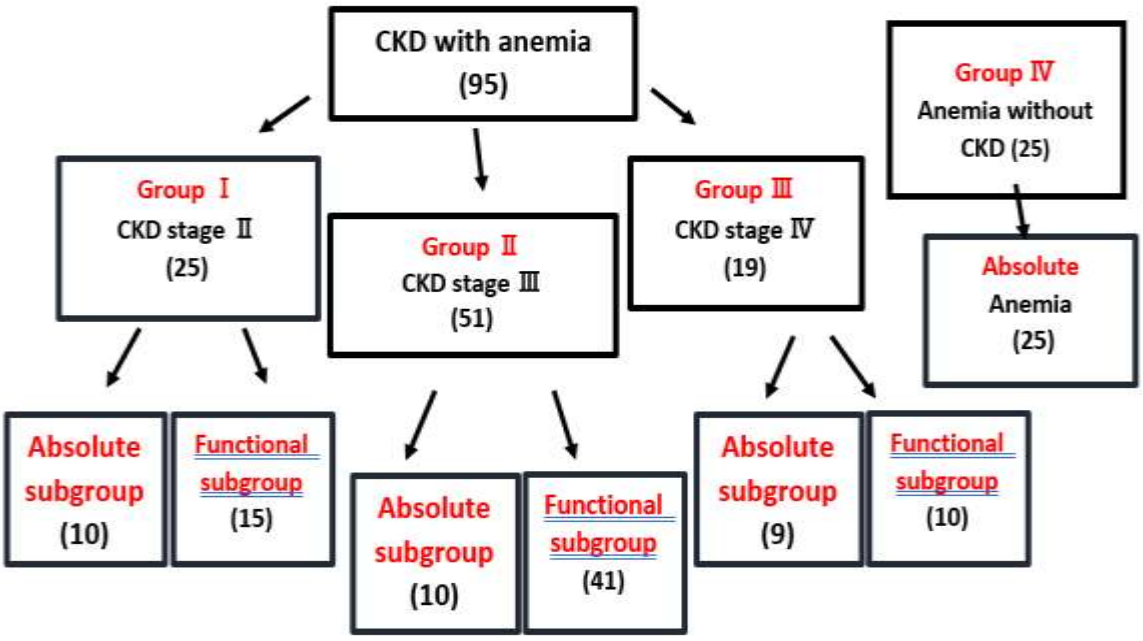

Fig.1 Examined children by groups and subgroups

Iron deficiency is considered one of the causes of anemia in children with chronic kidney disease. Serum iron in the examined children with absolute anemia was 7.07±0.45 ($p<0.05$); 6.23±0.34 ($p<0.05$) and 4.61±0.34 ($p<0.05$) μmol/L in the groups, while in children with functional anemia, the results were 9.16±0.88 ($p<0.05$); 7.18±0.32 ($p<0.05$) and 5.30±0.26 ($p<0.05$) μmol/L. This indicates that with the progression of the CKD stage, there is a decrease in serum iron in both absolute and, more significantly, functional anemia due to the intensive use of iron for the production of red blood cells, leading to the depletion of iron stores in the body (Table 1).

The level of serum ferritin is used to assess these iron stores in the body. A decrease in blood ferritin was observed in patients with absolute anemia to 63.22±5.06; 52.46±3.7 ($p<0.05$); 40.08±3.3 ($p<0.05$) μg/L in groups I, II, and III respectively, due to the increased need for iron for hemoglobin and erythrocyte synthesis. In patients with functional

anemia, this indicator increased, reaching 105.59±6.23 ($p < 0.05$); 132.94±4.64 ($p < 0.05$) and 162.67±8.94 ($p < 0.05$) μg/L in groups I, II, and III, indicating the mobilization of iron stores and activation of ferritin synthesis in functional anemia.

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Table 1

Hemodynamic Blood Indicators in Children by Type of Anemia

Indicator	Healthy, M±m	Group I, M±m		Group, II M±m		Group, III M±m		Group IV, M±m
		A	F	A	F	A	F	
Serum iron, μmol/L	16,5±0,38	7,07±0,45 p <0,05	9,16±0,88 p <0,05	6,23±0,34 p <0,05	7,18±0,32 p <0,05	4,61±0,34 p <0,05	5,30±0,26 p <0,05	14,34±0,74
Ferritin, μg/L	90,5±0,21	63,22±5,06	105,59±6,23 p <0,05	52,46±3,7 p <0,05	132,94±4,64 p <0,05	40,08±3,3 p <0,05	162,67±8,94 p <0,05	82,5±6,46
Transferrin, g/L	2,8±0,56	2,89±4,74 p <0,05	2,59±0,06 p <0,05	3,27±0,17 p <0,05	2,02±0,12	4,02±0,3 p <0,05	1,51±0,06 p <0,05	2,32±0,08
Erythropoietin, mIU/mL	17,8±12,2	39,41±3.2 p <0,05	5,40 ±0,76 p <0,05	50,26±8,73 p <0,05	5,06±0,61 p <0,05	55,85±1,96 p <0,05	2,43±0,43 p <0,05	24,05±0,65
Hepcidin, ng/mL	40,5±0,01	57,37±4,34 p <0,05	117,04±13,7 p <0,05	67,07±5,2 p <0,05	203,10±8,72 p <0,05	81,38±3,69 p <0,05	385,38±26,5 p <0,05	47,95±2,85

Note: p - reliability of differences between the results of iron metabolism indicators in blood and indicators in healthy individuals

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Significantly high levels of transferrin, which characterize the body's compensatory response to iron deficiency, were noted to a greater extent in groups II and III in children with absolute anemia, amounting to 3.27±0.17 ($p < 0.05$) and 4.02±0.3 ($p < 0.05$) g/L. Meanwhile, in functional anemia, transferrin concentration had low values in groups II and III (2.02±0.12 ($p < 0.05$) and 1.51±0.06 ($p < 0.05$) g/L), which in turn indicates the absence of iron for transferrin to transport.

Stimulation of erythropoietin (EPO) production is aimed at compensating for anemia to improve oxygen transport in response to hypoxia. Accordingly, EPO increased its values in children with absolute anemia to 39.41±3.2 ($p < 0.05$); 50.26±8.73 ($p < 0.05$) and 55.85±1.96 mIU/mL in groups I, II, and III respectively. Whereas the results for functional anemia were 5.40±0.76 ($p < 0.05$); 5.06±0.61 ($p < 0.05$) and 2.43±0.43 ($p < 0.05$) mIU/mL in the groups, indicating a complete lack of EPO and its production by the kidneys in children with anemia of chronic disease (ACD) (Fig.2).

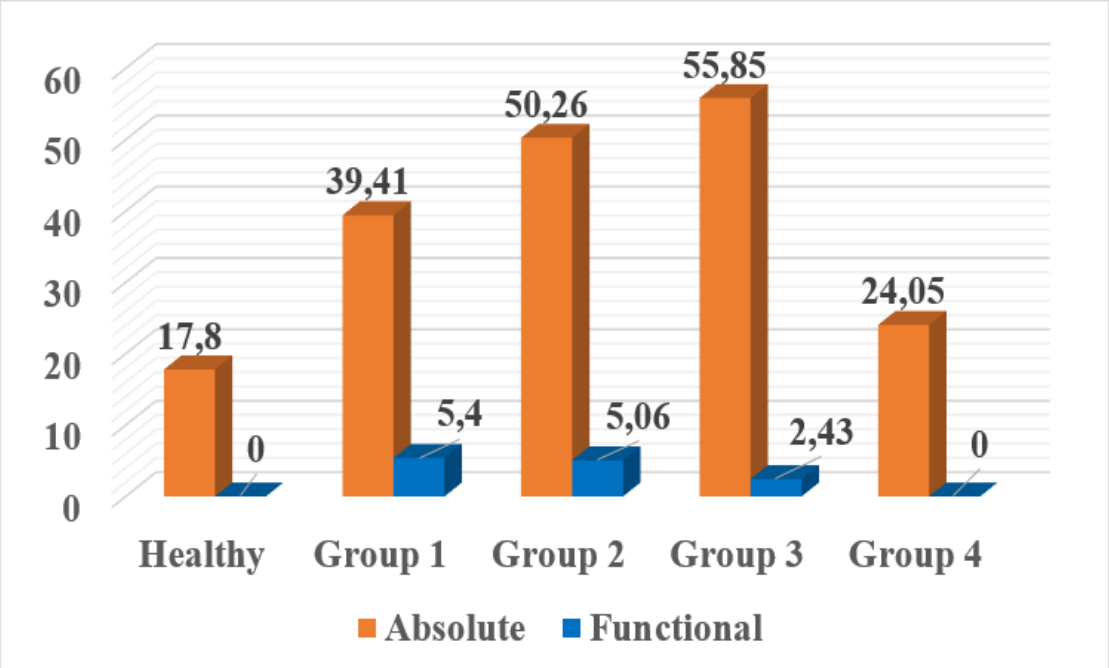

Fig.2 Comparison of erythropoietin levels in groups of children with absolute and functional anemia

Hepcidin, as a hormone controlling iron levels in the body, increased in 80% (76) of the examined children, indicating iron metabolism dysfunction, leading to anemia by limiting iron absorption from the intestine and reducing its availability for erythrocyte formation in the bone marrow. In absolute anemia, its concentration remained within the high normal range: 57.37±4.34 ng/mL; 67.07±5.2 ng/mL; 81.38±3.69 ng/mL in groups I, II, and III, respectively. In functional anemia, the hepcidin level was higher: 117.04±13.7

ng/mL; 203.10±8.72 ng/mL; 385.38±26.5 ng/mL in groups I, II, and III, respectively, indicating a disrupted regulation of iron metabolism (Fig.3).

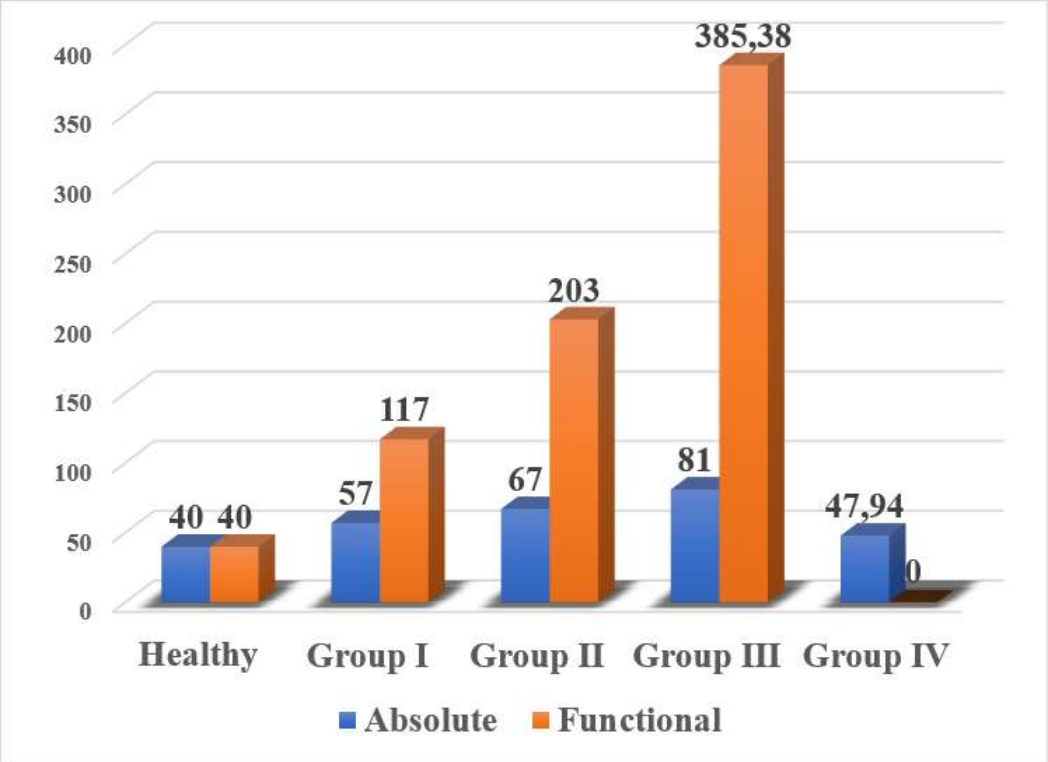

Fig.3 Comparison of hepcidin levels in groups of children with absolute and functional anemia

IL-6 is the main inflammation cytokine, playing a key role in increasing hepcidin levels, which subsequently leads to iron deficiency. TNF-α is a cytokine that suppresses the synthesis of erythropoietin and also contributes to the reduction of iron absorption from food, leading to its deficiency for erythrocyte formation.

Inflammation markers remained at normal levels in the subjects with absolute anemia. IL-6 levels in the groups were 6.79±0.6; 8.75±0.55 ($p<0.05$) and 10.47±0.94 pg/mL, and TNF-α was 2.62±0.4 pg/mL in group I; 4.69±0.36 pg/mL in group II; and 8.3±0.57 ($p<0.05$) pg/mL in group III (Table 2).

Table 2

Markers of blood inflammation depending on the type of anemia in children with CKD

Groups	Subgroups	Interleukin-6, pg/ml	TNF-α, pg/ml
Healthy, M±m		5,5±0,1	2,5±0,25
Group I, M±m	A	6,79±0,6	2,62±0,4
	F	14,29±0,88 (p <0,05)	11,26±0,57 (p <0,05)
Group II, M±m	A	8,75 ±0,55 (p <0,05)	4,69±0,36 (p <0,05)

	F	17,04±0,4 (p <0,05)	17,58±0,72 (p <0,05)
Group III, M±m	A	10,47±0,94	8,3±0,57 (p <0,05)
	F	21,09±1,55 (p <0,05)	20,7±1,33 (p <0,05)
Group IV, M±m		5,46±0,26	2,66±0,16

Note: p - significance of differences between cytokine blood parameters and parameters in healthy individuals

An increase in the cytokine profile was noted in 73% (70) of the subjects, which proves the functional nature of anemia in CKD. In group I, the concentration of IL-6 was 14.29±0.88 ($p<0.05$) pg/mL; in Group II, it was 17.04±0.4 ($p<0.05$) pg/mL; and in group III, it reached 21.09±1.55 ($p<0.05$) pg/mL. TNF-α increased its values in groups I, II, and III to 11.26±0.57 ($p<0.05$); 17.58±0.72 ($p<0.05$) and 20.7±1.33 ($p<0.05$) pg/mL, respectively. This confirms the severity of the inflammatory process, with a more pronounced degree in children in Group III with functional anemia.

4. Conclusion

Decreased levels of serum iron in association with low ferritin and below-average hemoglobin levels are indicators of iron-deficient hematopoiesis (absolute anemia). The concentration of hepcidin and cytokine parameters in this type of anemia remains within normal limits, while transferrin and erythropoietin increase their values for compensatory purposes. In the group of children with high ferritin levels, low serum iron, and transferrin values, the most pronounced are those with a functional type of anemia. Erythropoietin in this type of anemia tends to decrease significantly, while the levels of hepcidin and inflammation markers increase, and the higher the stage of CKD, the more significant their concentration becomes.

Thus, analyzing the aforementioned results, it can be noted that anemia in CKD in children has both absolute and functional characteristics. There are significantly different values of iron metabolism indicators (serum iron and ferritin, transferrin), hemoregulation hormones (erythropoietin and hepcidin), and cytokine profile (IL-6 and TNF-α) in children with each type of anemia at different stages of CKD, and as the stage of the disease increases, the concentration of these blood parameters changes. Functional anemia, as anemia of chronic diseases, in children is more severe compared to absolute anemia. Therefore, it is necessary to conduct laboratory diagnostics for all CKD patients and to start it at the early stages of the disease to determine the nature of the anemia. Subsequently, a more thorough approach to the treatment of functional anemia is required, regardless of absolute anemia, depending on the stage of development of chronic kidney disease in children.

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