

## THE EFFECT OF CHRONIC CONCOMITANT ANEMIA ON HEART FAILURE AND DIABETES MELLITUS

**Normatov Murod Buribayevich**

*Samarkand State Medical Institute*

*Assistant of the Department of Propaedeutics of Internal Diseases,*

*Samarkand, Uzbekistan*

**Xaydaraliyeva Soliha Utkirovna**

*Samarkand State Medical University Faculty of treatment student group 520*

**Umirkulov Hasan Axrorovich**

*Samarkand State Medical University Faculty of treatment student group 520*

**Dilmurodova Muxlisa Berdimurodovna**

*Samarkand State Medical University Faculty of treatment student group 520*

**Abstract** *The clinical significance of iron deficiency in patients with combined heart failure and diabetes mellitus remains poorly understood. In this study, 67 patients with chronic heart failure and diabetes mellitus were examined. Clinical symptoms of heart failure, asthenia, anxiety, and depression were assessed, as well as laboratory parameters including blood glucose, glycated hemoglobin, serum iron, ferritin, transferrin, soluble transferrin receptors, and hepcidin levels. Additionally, the levels of erythropoietin and NT-proBNP were measured. Echocardiographic examination was performed using one-dimensional, two-dimensional and Doppler methods (including pulse wave, continuous wave and tissue Doppler imaging) under standard conditions in accordance with established protocols. Iron deficiency was detected in 42 patients. The data obtained indicate that iron deficiency in patients with both heart failure and diabetes mellitus is associated with disruptions in iron metabolism, an increase in the severity of heart failure symptoms, greater asthenia and anxiety, and deterioration in central hemodynamic function.*

**Keywords:** *heart failure, diabetes mellitus, iron deficiency*

### INTRODUCTION

A common concomitant pathology in patients with chronic heart failure (CHF) is diabetes mellitus (DM). According to various authors, diabetes and even prediabetes are factors contributing to the development of chronic heart failure (CHF). In addition, diabetes worsens the prognosis in patients with CHF. In particular, patients with CHF and DM have an increased risk of hospitalization and death. Another common pathology in patients with CHF is iron (ID) deficiency. The latter significantly worsens the clinical condition of such patients and the prognosis. Many patients with CHF have a combination of these comorbid conditions. At the same time, there is no data on the clinical significance of ID in patients with comorbid CHF and diabetes. The purpose of the work to establish the clinical significance of iron deficiency in patients with CHF in combination with diabetes.

## MATERIALS AND METHODS OF RESEARCH

There were 67 patients with CHF and type 2 diabetes, with an average age of  $70.33 \pm 8.32$  years, under observation in the therapeutic department. All those included in the study underwent a comprehensive examination, including a clinical examination with an assessment of the clinical condition scale (SHOCK), a 6-minute walking test (T6M). Echocardiography was performed in all patients (ECHO-KG) on the GEVIVID-7 device in one-dimensional, two-dimensional and Doppler modes (pulse-wave, constant-wave and tissue) in standard positions according to the generally accepted method with the determination of the size and volume of the ventricles and atria, ejection fraction, regurgitation rate on the valves, transmitral diastolic flows, systolic pressure in the pulmonary artery (SDLA), the velocity of the fibrous ring of the mitral and tricuspid valves (SDFC-TC). All patients underwent a general blood test with determination of erythrocyte indices. The concentration of iron in mmol/l, transferrin in g/l, ferritin in mg/l, C-reactive protein (in mg/l) in blood serum was determined by highly sensitive The iron transferrin saturation coefficient (CNTF) was calculated using the photometric endpoint method. By the enzyme immunoassay on an ELISA reader Immunochem-2100 (USA) measured the level of the N-terminal fragment of the brain natriuretic

peptide in pg/ml, erythropoietin in IU/ml, soluble transferrin receptors (RRTP) in nmol/l, and hepcidin in ng/ml. Iron deficiency was established based on the recommendations of the European Society of Cardiology. It was determined by conventional methods in the blood. The levels of glucose, glycated hemoglobin, creatinine, and glomerular filtration rate (GFR) were calculated using the SKD-EPI formula. To assess the presence and severity of asthenia, the MFI-20 asthenia scale was used with an assessment in points of such manifestations of asthenia as general asthenia (OA), physical asthenia (FA), mental asthenia (PA), decreased motivation (CM), decreased activity (PA), total score of asthenia (CA). To determine the presence of anxiety and depression, use the HADS hospital scale of anxiety and depression in points. One-factor analysis of variance was used to compare the averages of the two samples. The Chi-square criterion was used to determine the differences in qualitative characteristics. To assess the relationship between different parameters, the gamma correlation coefficient was calculated. The level of reliability of the differences was assumed to be  $p < 0.05$ .

## THE RESULTS AND THEIR DISCUSSION

Depending on the presence of iron deficiency, based on the level of ferritin  $< 100$  mcg/l, all the examined were divided into two groups: Group 1 – patients without ID (25 people) and group 2 – patients with ID (42 people). There were no significant differences in the proportion of patients with different CHF FC in the compared groups ( $p > 0.05$ ): 2 FC – 31%, 3 FC – 44%, 4 FC – 25% in group 1 versus 19, 52 and 29% in group 2 with 2, 3 and 4 FC, accordingly. The test was crucial in determining CHF FC. A 6-minute walk is the most objective criterion. Patients of the 1st and 2nd groups did not have reliable differences ( $p > 0.05$ ) in age, weight, body mass index, glucose, glycated hemoglobin, creatinine, and GFR. In the group of patients with ID, along with a low ferritin level, the concentration of iron and the content of soluble transferrin receptors were significantly lower and higher. In addition,

patients with ID have significantly lower hemoglobin levels in the blood, the average hemoglobin content in the red blood cell, and a higher concentration

of erythropoietin. There were no significant differences in the number of red blood cells, as well as other indicators of the total blood count, in the compared groups.

Comparison of clinical status and echocardiography in groups of patients with CHF and SD combined with and without ID has shown that Patients with ID have higher SHOCK and SDL scores and lower left ventricular ejection fraction and SDFC-TC. In addition, patients with ID have higher manifestations of asthenia such as OA, FA, PAK, SM, PA, CA, and anxiety. Despite the fact that, as noted above, there are significant differences in the frequency of occurrence of patients with various CHF FC in the groups with the presence and absence of There was no ID, and the distance traveled in T6M in the group with ID was slightly lower than

in patients without ID. In the group of patients as a whole, reliable ( $p < 0.05$ ) correlations were established between the parameters characterizing iron metabolism and clinical indicators. In particular, significant positive correlations were found between the concentration of iron in the blood and the distance traveled in T6M. (0.40), stroke volume (0.40) and velocity of the tricuspid valve fibrous ring (0.28) and negative correlations between iron levels and SHOCK scores (-0.53), LP size (-0.25), SDLA (-0.29), anxiety (-0.34) and all manifestations of asthenia: OA (-0.28), FA (-0.28), PA (-0.34), CM (-0.38), PS (-0.35), the total indicator of asthenia (-0.36). In addition, significant ( $p < 0.05$ ) positive correlations between the level of RRTP were established. and SHOCK scores (0.66), SDLA value (0.53), left atrium size (0.60), severity FA (0.62), CM (0.59), and the total severity of asthenia (0.55). There were also significant ( $p < 0.05$ ) positive correlations between CTJ and the distance traveled in T6M (0.42) and stroke volume (0.33) and negative significant correlations between CTJ and SHOCK scores (-0.53), LP size (-0.32), SDLA (-0.28), anxiety (-0.32) and almost all manifestations of asthenia: FA (-0.26), OA (-0.29), CM (-0.35), PA (-0.32), CA (-0.33). Thus, patients with J who are comorbid in CHF and DM have significant abnormalities in iron metabolism, compared with patients with CHF and SD without J. In patients with J, in addition to a significant decrease in ferritin levels, indicating a sharp decrease in iron reserves in the body, significantly lower iron levels are observed. There is also a lower iron saturation coefficient in the blood, reflecting insufficient supply of tissues with iron. In such patients, the concentration of soluble transferrin receptors is significantly higher, which is an indicator of increased tissue iron demand. In patients with J, the level of erythropoietin is also increased, the production of which increases under the influence of a factor formed in tissues during hypoxia. Despite the fact that the average hemoglobin index in the group with J. was almost normal, the hemoglobin level and the average hemoglobin content in the erythrocyte in this group were slightly lower than in patients without J. Against this background, patients with CHF and DM who are comorbid have more pronounced clinical manifestations of heart failure than patients with the same comorbid pathology without JH. In particular, patients with JD have higher SHOCK scores, lower left ventricular ejection fraction, lower tricuspid valve fibrous ring velocity, and higher systolic pressure in the pulmonary artery. It can be assumed that these differences are to some extent related to a reduced level of iron reserves in

the body. and, in particular, in cardiomyocytes and muscles, since it is known that the iron content in the myocardium of patients with heart failure can be reduced by 20-30%. At the same time, it is known that iron plays an important role in oxygen transport and metabolism of cardiac and skeletal muscles. Patients with JH have more pronounced various manifestations of asthenia and anxiety. These features may be due to both more pronounced manifestations of CHF in such patients and disorders

of iron metabolism. At the same time, activation of the sympathetic nervous system accompanies anxiety, it may itself contribute to the development of iron metabolism disorders. The found that an increase in the level of norepinephrine in patients with CHF contributes to a decrease in transferrin iron saturation  $<20\%$  and an increase in the level of soluble transferrin receptors. The importance of iron metabolism disorders in exacerbating clinical manifestations in patients with CHF and DM is confirmed by the presence of reliable correlations of iron metabolism parameters with clinical and echocardiographic indicators. In particular, these are

positive correlations between concentration iron and T6M, stroke volume and velocity of the tricuspid valve fibrous ring, and negative correlations between iron levels and SHOCK scores, left atrium size, SDL, anxiety, and severity of asthenia. This is also evidenced by the positive correlations between CSTJ and T6M and stroke volume and negative significant correlations between CSTJ and scores SHOCK, the size of the left atrium, SDLA, anxiety, and all manifestations of asthenia. The importance of iron metabolism disorders with a deficiency of its reserves in the body for the deterioration of patients with CHF and DM The positive correlations between the level of RRTP and SHOCK scores, the value of SDLA, are also confirmed., the size of the lesion and the severity of asthenia.

### **CONCLUSIONS**

With a deficiency of iron reserves in the body in patients with CHF and DM, there is a decrease in the concentration of iron in the blood, a decrease in the iron saturation coefficient of transferrin and an increase in soluble transferrin receptors, as well as a slight decrease in hemoglobin levels and the average hemoglobin content in the red blood cell. Against this background, the clinical manifestations of CHF, asthenia and anxiety are increasing, as well as some echocardiographic indicators are deteriorating. The data obtained indicate the importance of early detection of GI in patients with comorbidity CHF and DM for possible subsequent correction disorders of iron metabolism.

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