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NEW DAY IN MEDICINE**

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## ANALYSIS OF BIOCHEMICAL AND HEMATOLOGICAL INDICATORS IN CHRONIC LIVER DISEASES

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### ✓ *Resume*

**Target.** To analyze the state of biochemical and hematological parameters in chronic liver diseases. **Material and methods.** The material for the study included 156 patients with CKD (1st main group) and 80 healthy patients without liver disease (4th comparison control group). The median age of those examined was 53.3±1.4 years. Among all the studied individuals, biochemical and hematological blood tests were carried out to determine the content of ferritin, vitamin B12 and folic acid in the blood serum (biochemical and hematological automatic analyzers “Mindray, China”). Statistical calculations of the obtained results were carried out using the statistical software package “OpenEpi 2009, Version 9.2”. **Conclusions:** signs of worsening liver damage, in particular with cirrhosis, in biochemical and general blood tests are more pronounced changes in the presented indicators, which are very important laboratory signs that make it possible to prevent the worsening of the disease in the early stages of the development of cirrhosis through their timely correction.

**Key words:** chronic liver diseases, chronic hepatitis, liver cirrhosis, biochemical changes, hemogram, severity.

### Relevance

Chronic liver diseases (CLD), characterized by the heterogeneity of causative factors that complicate their early diagnosis, have the status of one of the global health problems around the world [1, 2, 8,12].

In accordance with the data of the World Health Organization (WHO), in recent years, CLD affects 1.5 billion of the world's population, among which the highest levels are occupied by CLD of non-viral etiology (60%) and viral etiology (38%) [3,4]. At the same time, according to European and Asian studies, the standardized incidence rate of CLD by age in the world is within 20.7 per 100,000 population, in European countries - 26.0/100,000, and in Asian countries from 16.5 to 23.6/100,000 [5,7,10].

Research results assessing the problem of mortality in CLD show that a tendency to increase this indicator with LC per 100,000 population is observed in almost all regions of the world [6,9,11].

Advances achieved in understanding the pathogenetic basis of the formation of CLD through the results of clinical and experimental studies have made it possible to uncover new mechanisms underlying their onset [3,5,9,11]. Meanwhile, there are still many open questions with no clear answers regarding the complex genesis of CLD, which confirms the need to continue research in this area.

**Purpose of the study:** To analyze the state of biochemical and hematological parameters in patients with chronic liver diseases.

### Material and methods

The studies were conducted on the basis of a random sample of patients aged from 19 to 79 years (median age 53.0±5.8 years), with chronic liver diseases of viral origin, who were hospitalized at the Khorezm Regional Multidisciplinary Medical Center (KRMMC) from 2019-2023. The number of patients included in the study was 156 patients, among whom 75 had chronic hepatitis (CH) and 81 had liver cirrhosis (LC).

The control group included relatively healthy adults (median age  $51.1 \pm 4.3$  years) without pathologies in the hepatobiliary system and other inflammatory diseases ( $n=80$ ).

Verification of the diagnosis was carried out according to the standards for diagnosing liver diseases. All patients who gave informed consent to participate in the study were under observation and inpatient treatment with chronic liver diseases at the Khorezm Regional Multidisciplinary Medical Center (Urgench) from 2020 to 2023.

The list of biochemical blood parameters included determination of the amounts of total protein and albumin, ALT and AST transaminases, alkaline phosphatase, total, direct, free and urea bilirubin. The content of ferritin, vitamin B12 and folic acid in the blood serum was determined separately (biochemical automatic analyzer "Mindray, China").

General blood test indicators included: hemoglobin, red blood cells, color index, platelets, leukocytes, leukocyte formula, % (Hematology automatic analyzer "Mindray, China") and ESR, mm/h (2-15) (Panchenkov apparatus, Russia). Statistical calculations of the obtained results were carried out using the statistical software package "OpenEpi 2009, Version 9.2".

### Results and discussion

In our study, the results of biochemical analysis in patients with CKD revealed changes confirming the presence of liver dysfunction.

Among the first indicators showing impairment of synthetic liver function in patients in the main group with CKD were a decrease in the total protein and albumin content from the median of acceptable normal values by 1.26 ( $59.7 \pm 7.9$  g/l;  $P > 0.05$ ) and 1.32 ( $33.3 \pm 5.61$  g/l;  $P > 0.05$ ) times, respectively.

Along with this, assessing these indicators in patients with chronic hepatitis and cirrhosis, their decrease was also revealed. Thus, if the content of total protein in these groups decreased compared to the median norm by 1.17 ( $64.0 \pm 1.02$ ;  $P > 0.05$ ) and 1.4 ( $55.7 \pm 0.8$ ;  $P > 0.05$ ) times, then the amount of albumin decreased by 1.12 ( $39.2 \pm 0.7$ ;  $P > 0.05$ ) and 1.6 ( $27.9 \pm 0.3$ ;  $P < 0.05$ ) respectively times. At the same time, the amount of total albumin protein in CG varied from 82 g/l to 50.2 g/l and 52.1 g/l to 27 g/l, and in cirrhosis - from 71.0 g/l to 42.0 g/l and from 34.1 g/l to 22.0 g/l. Based on these results, the natural fact of a more pronounced decrease in the synthetic function of the liver in the group of patients with cirrhosis is obvious.

At the same time, the presence of activity of the inflammatory process in the liver in the main group of patients with CLD was evidenced by an increase in the concentration of total bilirubin by 2.65 ( $31.7 \pm 4.3$   $\mu\text{mol/l}$ ;  $P < 0.01$ ), its bound and free fractions by 3.2 ( $19.6 \pm 2.73$   $\mu\text{mol/l}$ ;  $P < 0.001$ ) and 1.3 times ( $12.1 \pm 3.31$   $\mu\text{mol/l}$ ;  $P > 0.05$ ).

In the group with hCG, the content of total bilirubin and its fractions was also higher than the median norm of 2.3 ( $27.8 \pm 2.7$   $\mu\text{mol/l}$ ;  $P < 0.01$ ); 2.6 ( $16.1 \pm 1.6$   $\mu\text{mol/l}$ ;  $P < 0.01$ ) and 1.24 times ( $11.7 \pm 0.7$   $\mu\text{mol/l}$ ;  $P > 0.05$ ). Meanwhile, in patients with cirrhosis, the median of total bilirubin and its fractions from the median of the norm respectively increased by 2.95 ( $27.8 \pm 2.7$   $\mu\text{mol/l}$ ;  $P < 0.001$ ); 3.9 ( $16.1 \pm 1.6$   $\mu\text{mol/l}$ ;  $P < 0.001$ ) and 1.2 times ( $11.7 \pm 0.7$   $\mu\text{mol/l}$ ;  $P > 0.05$ ).

In addition, in all groups of patients there was a high level of hepatocyte cytolysis, the indicator of which was an increase in liver transaminases ALT by 2.8 ( $55.3 \pm 9.1$  U/l;  $P < 0.01$ ); 2.8 ( $55.8 \pm 5.4$  U/l;  $P < 0.01$ ) and 2.91 times ( $58.3 \pm 3.4$  U/l;  $P < 0.01$ ) and AST 2.5 ( $44.2 \pm 7.9$  U/l;  $P < 0.01$ ); 2.46 ( $43.2 \pm 4.4$  IU/l;  $P < 0.01$ ) and 3.02 times ( $52.9 \pm 2.3$  IU/l;  $P < 0.001$ ) respectively in the groups of patients with CKD, CH and cirrhosis.

As well as in relation to the amount of total protein and albumin, in terms of bilirubin and liver transaminases, a more pronounced imbalance was characteristic of patients with cirrhosis.

Analyzing the median LDH values, a statistically insignificant increase in the median LDH from the upper acceptable limit of normal was found in all groups with greater severity in cirrhosis ( $485.9 \pm 3.9$  U/l;  $P > 0.05$ ), which indicated a greater severity of hepatocyte cytolysis in this group of patients. Regarding the indicator of cholestasis - ALP, enzyme activity remained within normal limits in all groups of patients (CKD -  $171.2 \pm 11.5$  U/l; CG -  $162.6 \pm 2.3$  U/l and CP -  $179.1 \pm 3.2$  U/l).

An indicator providing information about the impairment of the detoxification function of the liver was a decrease in urea levels, compared with the median norm of this indicator in the group of patients with cirrhosis by 1.6 times ( $2.8 \pm 0.9$  mmol/l;  $P < 0.05$ ).

Assessing the indicators in the general blood test in the main group of patients with CKD in relation to the median of normal values, the presence of anemia was discovered, expressed as a moderately severe decrease in hemoglobin to  $86.2 \pm 10.5$  g/l and red blood cells to  $3.33 \pm 2.1 \times 10^{12}/l$ .

Similar dynamics of decrease in hemoglobin and erythrocytes were observed in the group with hCG, where the median hemoglobin decreased to  $91.5 \pm 1.5$  g/l, and erythrocytes to  $3.4 \pm 0.05 \times 10^{12}/l$ .

In the group of patients with cirrhosis, the decrease in hemoglobin ( $81.3 \pm 1.03$  g/l) and erythrocytes ( $3.3 \pm 0.5 \times 10^{12}/l$ ) was more noticeable.

A hematological indicator related to the depth of liver damage is the number of platelets, the average number of which in the group with CKD decreased from the median norm statistically significantly by 2.0 times ( $149.2 \pm 24.3 \times 10^{12}/l$ ;  $P < 0.01$ ), with CG being within the normal range by 1.5 times ( $196.8 \pm 3.5 \times 10^{12}/l$ ;  $P > 0.05$ ) and among patients with cirrhosis in 2.8 times ( $105.1 \pm 3.05 \times 10^{12}/l$ ;  $P < 0.01$ ).

The median of leukocytes, also depending on the severity of liver damage, tended to decrease relative to the median of their norm in the main group with CKD by 1.3 times ( $5.8 \pm 2.2 \times 10^{12}/l$ ;  $P > 0.05$ ), in patients with chronic hepatitis by 1.26 ( $6.1 \pm 0.2 \times 10^{12}/l$ ;  $P > 0.05$ ) and in patients with cirrhosis by 1.37 times ( $5.6 \pm 0.2 \times 10^{12}/l$ ;  $P > 0.05$ ).

Along with this, an important indicator characterizing the presence of inflammatory process activity was the acceleration of ESR in all groups of patients. Thus, in the main group, relative to the median in normal conditions, ESR was accelerated by 1.6 times ( $13.5 \pm 2.2$  mm/h;  $P < 0.05$ ), with CG by 1.3 ( $10.7 \pm 0.6$ ;  $P > 0.05$ ) and with CP by 1.9 times ( $16.1 \pm 1.03$ ;  $P < 0.05$ ).

Analysis of the average values of the leukocyte formula and erythrocyte indices showed the absence of significant fluctuations from their normal values.

In the general group of patients, the percentage of neutrophils was 60.5%, lymphocytes - 32.1%, monocytes - 6.5%, eosinophils - 0.76 and basophils - 0.16%.

Along with the absence of deviations of these indicators from the norm, in the groups of patients with chronic hepatitis and cirrhosis, leukoformula indicators were determined with almost similar dynamics.

Analyzing the dynamics of the average values of erythrocyte indices in groups of patients with CLD, no sharp deviations from their normal values were found.

The absence of shifts from normal values in the MCH and MCHC parameters with a simultaneous increase in MCV parameters indicated the presence of normochromic and macrocytic anemia in patients with CLD.

In addition to assessing the indicators of a general blood test in patients with CLD, to clarify the nature of anemia, it seemed interesting to us to evaluate the serum levels of ferritin, folic acid and cyanocobalamin both in the general group of patients with CLD, and in CG and cirrhosis separately.

Analyzing the concentration of ferritin in patients with CLD (CG and cirrhosis), their content was found to be within normal limits. Meanwhile, the median concentration of ferritin was higher than the median of its control level in the main group of patients by 1.4 ( $113.3 \pm 13.6$  nm/ml;  $P > 0.05$ ), in the groups with CG by 1.45 ( $118.0 \pm 3.4$  nm/ml;  $P > 0.05$ ) and CP by 1.34 ( $108.9 \pm 2.2$  nm/ml;  $P > 0.05$ ) times.

Most likely, the relative increase in ferritin in this case served as an indicator of active chronic inflammation in patients with CLD and did not reflect its true content outside the activity of the inflammatory process.

At the same time, assessing the serum content of folic acid in patients with CLD, its amount was found to be at a very low normal level, while calculations showed that from the control median in the main group of patients the amount of folic acid was statistically significantly reduced by 3.7 times ( $2.9 \pm 1.9$  nmol/l;  $P < 0.001$ ), with CG also by 3.7 ( $2.9 \pm 0.03$ ;  $P < 0.001$ ), and with cirrhosis by 3.8 ( $2.8 \pm 0.02$ ;  $P < 0.001$ ) times.

In patients with CLD compared to controls, a similar decrease was observed in the serum amount of cyanocobalamin, with its normal low level. In the main group, the indicator was statistically significantly lower than in the control by 3.64 ( $174.4 \pm 19.1$  pmol/l;  $P < 0.001$ ), with CG by 3.45 ( $183.6 \pm 1.7$  pmol/l;  $P < 0.001$ ) and with cirrhosis by 3.8 ( $165.9 \pm 3.2$  pmol/l;  $P < 0.001$ ) times.

Consequently, the differences in the levels of folic acid and cyanocobalamin between the groups of patients and controls indicate the presence of their significant decrease in CLD.

## Conclusion

Thus, assessment of the status of biochemical blood parameters in CKD made it possible to identify signs of decreased synthetic (decreased total protein and albumin) and detoxification liver function (LC), accompanied by the presence of cytolytic syndrome (increased bilirubin concentration, ALT, AST and LDH activity), the severity of which depended on the severity of liver damage.

At the same time, in the hematological indicators of a general blood test for chronic liver diseases, a number of changes are characteristic, manifested by a decrease in hemoglobin, red blood cells, platelets and leukocytes with an acceleration of the ESR rate.

The detected mild anemia in patients with chronic hepatitis ( $91.5 \pm 1.5$  g/l) and moderate anemia in patients with cirrhosis ( $81.3 \pm 1.03$  g/l) more often had a macrocytic normochromic character, confirmed by a decrease in the median MCV and RDW with normal values of MCH and MCHC.

At the same time, the mechanism of development of anemia in CKD is diverse and it is quite difficult to track its root cause in patients, because The pathogenesis of anemia in liver pathologies, in addition to a decrease in the synthetic function of the liver, consists of disturbances in the maturation processes and proliferation of bone marrow cells (erythrocytes, platelets and leukocytes) both due to disturbances in the metabolism of folate, cyanocobalamin, iron, and increased destruction of erythrocytes and other blood cells in the spleen.

Along with this, it is important to emphasize that signs of worsening liver damage, in particular with cirrhosis, in biochemical and general blood tests are more pronounced changes in the presented indicators, which are very important laboratory signs that allow, in the early stages of the development of cirrhosis, to prevent the worsening of the disease through their timely correction.

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