FACTORS INFLUENCING LIVER CHANGES

F. Kh. Umarov
Bukhara State Medical Institute

Annotation: *The formation of cirrhosis of the liver occurs over many months or years. During this time, the gene apparatus of hepatocytes changes and generations of pathologically altered cells are created. This process in the liver can be characterized as immunoinflammatory. The most important factor in the genesis of alcoholic cirrhosis of the liver is damage (necrosis) of hepatocytes due to the direct toxic effect of alcohol, as well as autoimmune processes. Sensitization of immunocytes to the body's own tissues is an important factor in the pathogenesis of cirrhosis that develops in patients with viral hepatitis B, C and D.*

Keywords: *cirrhosis, the hepatitis B virus, hepatocellular function, the hepatitis C virus, the hepatitis D virus, dyspeptic syndrome*

Cirrhosis of the liver (LC) is a chronic polyetiological progressive disease that occurs with damage to the parenchymal and interstitial tissue of the organ with necrosis and degeneration of liver cells, nodular regeneration and diffuse proliferation of connective tissue, impaired organ architectonics and the development of varying degrees of liver failure.

In economically developed countries, cirrhosis of the liver is one of the six leading causes of death between the ages of 35 and 60, ranging from 14 to 30 cases per 100,000 population. In the world, 40 million people die annually from viral cirrhosis of the liver and hepatocellular carcinoma, which develops against the background of carriage of the hepatitis B virus. In the CIS countries, cirrhosis occurs in 1% of the population.

Etiology and pathogenesis

The most common causes of liver cirrhosis are chronic alcohol intoxication (according to various sources, from 40-50% to 70-80%) and viral hepatitis B, C and D (30-40%). The most important stages in the occurrence of alcoholic cirrhosis of the liver are acute alcoholic hepatitis and fatty degeneration of the liver with fibrosis and mesenchymal reaction. Alcohol-viral cirrhosis with a rapidly progressive course of the disease is characterized by a particularly severe course. They most often transform into hepatocellular carcinoma. Significantly less often in the development of cirrhosis of the liver, diseases of the biliary tract (intra- and extrahepatic), congestive heart failure, various chemical and drug intoxications play a role. Rare forms of liver cirrhosis are associated with genetic factors leading to metabolic disorders (hemochromatosis, hepatolenticular degeneration, a1-trypsin deficiency), and occlusive processes in the portal vein system (phleboportal cirrhosis). The cause of primary biliary cirrhosis remains unclear. In approximately 10–35% of patients, the

etiology of cirrhosis cannot be established. Such observations are referred to as cryptogenic cirrhosis, the causes of which are still unknown.

A further stage in the development of the pathological process: portal hypertension is an increase in pressure in the portal vein system due to obstruction of the intra- or extrahepatic portal vessels. Portal hypertension, in turn, leads to porto-caval shunting, splenomegaly, and ascites. Thrombocytopenia (increased deposition of platelets in the spleen), leukopenia, anemia (increased hemolysis of red blood cells) are associated with splenomegaly.

Ascites leads to restriction of diaphragm mobility (risk of pulmonary atelectasis, pneumonia), gastroesophageal reflux with peptic erosions, ulcers and bleeding from varicose veins of the esophagus, abdominal hernia, bacterial peritonitis, hepatorenal syndrome.

In patients with cirrhosis of the liver, hepatogenic encephalopathies are often observed.

The leading place in the origin of primary biliary cirrhosis of the liver belongs to genetic disorders of immunoregulation. The initial changes include the destruction of the biliary epithelium, followed by necrosis of the tubular segments and, at a later stage of the disease, their proliferation, which is accompanied by impaired bile excretion, the epithelium is infiltrated by lymphocytes, plasma cells, and macrophages. In the evolution of the disease, 4 stages are traced: chronic non-purulent destructive cholangitis, ductular proliferation with destruction of the bile ducts, scarring with a decrease in the bile ducts and the development of large-nodular cirrhosis and cholestasis.

Classification

The World Association of Hepatologists (Acapulco, 1974) and WHO (1978) recommended a simple morphological classification of liver cirrhosis, based on a minimum of criteria, according to which there are:

- fine-nodular, or fine-nodular (diameter of nodes from 1 to 3 mm);
- large-nodular, or macronodular (diameter of nodes more than 3 mm);
- incomplete septal;
- mixed (in which different sizes of nodes are observed) forms.

In accordance with the latest classification (Los Angeles, 1994), cirrhosis is distinguished by etiology, the degree of activity determined by biochemical tests (ALT activity), and morphological changes in the liver.

Depending on the etiology, liver cirrhosis is distinguished: viral, alcoholic, drug-induced, secondary biliary, congenital (hepatolenticular degeneration, hemochromatosis, a1-trypsin deficiency, tyrosinosis, galactosemia, glycogenosis), congestive (circulatory failure), Budd-Chiari disease and syndrome, metabolic - alimentary (imposition of bypass small bowel anastomosis, obesity, severe forms of diabetes mellitus) and cirrhosis of the liver of unclear etiology (cryptogenic, primary biliary, Indian children).

It is considered appropriate to divide liver cirrhosis depending on the severity of hepatocellular insufficiency (compensated, subcompensated, decompensated), the degree of portal hypertension and the activity of the process. Depending on the activity of the process, which refers to the severity of inflammatory reactions, all cirrhosis is divided into active and inactive.

Hepatocellular function in liver cirrhosis is assessed by Childe-Pugh

Compensated cirrhosis is indicated by the indicators of group A, the indicators of groups B and C correspond to decompensated cirrhosis (the technique of using criteria: one indicator of group A is estimated at 1 point, the same indicator of group B is two points, and in group C - 3 points). The proposed system is suitable for assessing the prognosis, especially without a sharp exacerbation of cirrhosis and its complications. In recent years, to determine the prognosis in patients with cirrhosis at the time of the development of such complications as gastrointestinal bleeding, coma, sepsis, etc., the SAPS (Simplifed Acute Physiology Score) criteria system is used, which includes the main physiological parameters, most of which are not directly related with the condition of the liver. These include: age, heart rate and respiration, systolic BP, body temperature, diuresis, hematocrit, white blood cell count, serum urea, potassium, sodium, and bicarbonate levels, hepatic coma stage

Clinical picture

Cirrhosis of the liver is more often observed in men: the ratio of male and female patients is on average 3:1. The disease occurs in all age groups, but more often after 40 years.

The complexity of early diagnosis of liver cirrhosis is largely due to the variety of its first clinical manifestations. The most common clinical manifestations include such general symptoms as weakness, decreased ability to work, discomfort in the abdomen, dyspeptic disorders, fever, joint pain. Flatulence, pain and a feeling of heaviness in the upper abdomen, weight loss, asthenia are often noted. On examination, an increase in the liver with compaction and deformation of its surface is revealed, the edge of the liver is pointed. In the initial stage, there is a uniform moderate increase in both lobes of the liver, in the future, an increase in the left lobe often predominates. Portal hypertension is manifested by moderate splenomegaly.

The period of the developed clinical picture is diverse in its symptoms and reflects the involvement of almost all body systems in the pathological process. The main, characteristic symptoms are associated with the presence of hepatocellular insufficiency and portal hypertension. The most common complaints are weakness, fatigue, decreased performance (bloating, poor tolerance to fatty foods and alcohol, nausea, vomiting, diarrhea), sleep disturbance, irritability. Especially often there is a feeling of heaviness or pain in the abdomen (mainly in the right hypochondrium), impotence, itching of the skin, menstrual irregularities in women. The most common objective symptom is hepatomegaly (70%). The liver has a compacted consistency, a pointed edge, little or painless. In 30% of patients, the nodal surface of the organ is

palpated. In the terminal stage of the disease in 25% of cases there is a decrease in the size of the liver, splenomegaly in 50% of patients.

External symptoms of cirrhosis are often found: palmar or plantar erythema, vascular "asterisks", sparse hair in the armpit and pubis, white nails, gynecomastia in men. These changes are explained by the appearance of signs of hyperestrogenemia against the background of hepatocellular insufficiency. Characterized by weight loss, often masked by the simultaneous accumulation of fluid. Half of the patients have elevated body temperature. In most cases, the fever is subfebrile in nature and persists for several weeks. The temperature associated with necrosis of hepatocytes is often accompanied by intense jaundice, increased activity of aminotransferases and serum alkaline phosphatase, and leukocytosis. An increase in temperature is associated with the passage through the liver of intestinal bacterial pyrogens, which it is not able to neutralize. The fever is not treatable with antibiotics and resolves only when liver function improves. Among the relatively late symptoms of cirrhosis, which characterize severe hepatocellular insufficiency and portal hypertension, include jaundice, ascites, peripheral edema (primarily swelling of the legs), external venous collaterals. Hepatolienal syndrome is often accompanied by hypersplenism, characterized by a decrease in blood cells (leukopenia, thrombocytopenia, anemia) and an increase in cellular elements in the bone marrow.

One of the most common signs in liver cirrhosis is varicose veins of the esophagus, stomach, intestines, including the duodenum, bleeding from which, due to the frequency of deaths, is the most serious complication of liver cirrhosis. Other venous collaterals, including mesenteric vessels, detected only by angiography or during surgery, can become a source of severe bleeding with a fatal outcome. Bleeding is also possible from the hemorrhoidal veins, but they are less common and less intense.

Encephalopathies occur both against the background of hepatocellular and against the background of portal-hepatic insufficiency.

Etiological variants of liver cirrhosis

Viral cirrhosis of the liver in most cases is macronodular. There are two variants of viral cirrhosis: early, developing within the first year after acute hepatitis (more often hepatitis D, which occurs with jaundice and a pronounced syndrome of cytolysis or cholestasis), and late, developing after a long latent period (5–15 years).

The clinical picture resembles the acute phase of viral hepatitis: jaundice, fever with chills, asthenovegetative and dyspeptic syndromes. Jaundice is moderate but persistent, hyperbilirubinemia persists constantly, despite ongoing therapy. The form of cirrhosis with cholestasis is accompanied by intense jaundice, persistent itching, and high levels of alkaline phosphatase. Peripheral abdominal collaterals do not have time to develop, there are no telangiectasias. Hepatomegaly is combined with splenomegaly. The marker of D-infection is the detection of anti-delta antibodies of the IgM and IgG classes. Late (more frequent) form of viral cirrhosis occurs gradually,

slowly in the outcome of chronic viral hepatitis B and C. Patients develop anorexia, heaviness in the right hypochondrium, flatulence, muscle and joint pain, nosebleeds, underweight, muscle wasting, dryness skin. Hepatomegaly, splenomegaly with hypersplenism, icteric skin, sclera, vascular "asterisks" and palmar erythema, portal hypertension and encephalopathy develop. Functional liver failure appears early and coincides with periods of exacerbation of the disease. In the stage of formed cirrhosis, dilated veins of the esophagus and hemorrhages are observed. Ascites joins in the later stages of the disease.

Alcoholic liver cirrhosis develops in approximately 10% of alcohol abusers within 5 to 20 years. Men get sick more often.

In the extended stage, dyspeptic complaints predominate - loss of appetite, vomiting, diarrhea. Dyspeptic syndrome is caused by concomitant gastritis and alcoholic pancreatitis. Much earlier than with viral cirrhosis, signs of dystrophy and beriberi are detected. Systemic exposure to chronic alcohol intoxication leads to polyneuritis, myopathy, muscle atrophy, Dipuytren's contracture, enlargement of the parotid glands, hair loss and testicular atrophy. In addition, alcoholism causes damage to the kidneys, heart, moderate arterial hypertension.

Secondary biliary cirrhosis of the liver develops as a result of a prolonged violation of the outflow of bile at the level of large intra- and extrahepatic bile ducts: with obstruction of the bile ducts by a stone, postoperative scar, benign tumors, it is also observed with primary sclerosing cholangitis, choledochal cysts, lymphogranulomatosis. The main pathogenetic links: initial cholestasis, perilobular fibrosis, cirrhosis. In connection with the mechanical obstruction of the biliary tract, biliary hypertension occurs and the flow of bile components into the periductal spaces is noted. The elimination of cholestasis contributes to the reverse development of the process. Biliary cirrhosis is characterized by pain, fever, chills, leukocytosis, hepatomegaly, splenomegaly, cholestasis syndrome - skin itching, severe jaundice, hyperbilirubinemia, elevated cholesterol, bile phosphatase, bile acids.

Primary biliary cirrhosis of the liver. The etiology is unknown in most cases.

The prevalence is 23-50 people per 1 million adults, among all cirrhosis of the liver is 6-12%. Mostly women during menopause get sick.

This gradually beginning progressive liver disease is characterized by granulomatous non-purulent destructive cholangitis with the development of fibrosis, cirrhosis. The first sign of the disease is itching, which is caused by an increased content of bile acids in the blood. Jaundice appears several years after the onset of itching. Characterized by skin pigmentation, xanthoma, xanthelasma, scratching. The liver is moderately enlarged, splenomegaly is determined in the later stages of the disease. With prolonged jaundice, systemic osteoporosis is detected: changes in the bones of the pelvis, skull, spine, ribs. Signs of portal hypertension (varicose veins of the esophagus, etc.) appear later than with common forms of liver cirrhosis. Of the biochemical tests, the highest diagnostic value has a high level of IgM and alkaline

phosphatase in the blood serum, hypercholesterolemia, hypertriglyceridemia. In 90% of cases, antibodies to mitochondria are noted.

Complications of cirrhosis of the liver

The most severe complications of cirrhosis of the liver: hepatic coma, bleeding from varicose veins of the esophagus (less often - the stomach, intestines), thrombosis in the portal vein system, hepatorenal syndrome, the formation of liver cancer. Often, especially with alcoholic cirrhosis, infectious complications are observed - pneumonia, "spontaneous" peritonitis with ascites (it is assumed that opportunistic intestinal bacterial flora plays an important role in its development - under the influence of edema of intestinal loops as a result of lymphostasis and impaired immunity, the intestinal flora penetrates into the free abdominal cavity and acquires clear pathogenic properties), sepsis.

Diagnosis of cirrhosis of the liver

Anamnestic data - alcohol abuse, past viral hepatitis B, C or D. Typical complaints of nosebleeds, dyspeptic disorders, weakness, abdominal pain, etc., make it possible to suspect the formation of liver cirrhosis in a patient.

In an objective study, the following indicators attract attention: telangiectasia in the shoulder girdle and face, erythema of the palmar and digital eminences, blanching of the nails, hemorrhagic diathesis, nutritional decline and atrophy of the skeletal muscles, grayish-pale skin tone or moderate icterus of the sclera, compacted liver with a sharp lower edge, splenomegaly, endocrine disorders.

The data of laboratory and instrumental research methods include: blood tests, leukothrombocytopenia, anemia, characteristic biochemical changes: hyper-g-globulinemia, hypoalbuminemia, increased activity of aminotransferases, hyperbilirubinemia due to the conjugated fraction of the pigment, etc., a decrease in the prothrombin index, other indicators of coagulation blood systems. Immunological methods for the study of blood serum are used to confirm one or another etiological form of liver cirrhosis. The concentration of immunoglobulins in active cirrhosis is usually increased, for alcoholic cirrhosis, an increase in the level of IgA is characteristic, for viral ones, predominantly IgG and IgM. A particularly significant increase in the concentration of IgM is observed in patients with primary biliary cirrhosis of the liver. In the same case, antibodies to mitochondria are detected in the blood serum. Among antimitochondrial antibodies, a number of fractions have been isolated, such as M-2 and M-9, the latter being given a special role in the early diagnosis of primary biliary cirrhosis.

The significance of instrumental research methods for this disease is different.

Ultrasound of the liver allows you to determine the size of the organs - the liver and spleen, the density of their parenchyma, visualize the presence of nodes and the spread of the process, and identify signs of portal hypertension.

Computed tomography is a more informative method, especially in patients with ascites and severe flatulence; allows you to get information about the density, homogeneity of the liver tissue; even small amounts of ascitic fluid are well captured.

Radionuclide scanning. Studies are carried out with colloid preparations 197Au and 99mTc. With cirrhosis of the liver, a diffuse decrease in the absorption of the isotope in the liver is observed. The method is uninformative.

Angiographic examination - celiacography and splenoportography. Used to visualize blood vessels and determine the presence and extent of portal hypertension.

Puncture biopsy of the liver is the most informative procedure, since it allows a histological examination of the biopsy, determine the type of pathological process and its stage.

Laparoscopic examination of the abdominal cavity, despite its traumatic nature in these patients, provides additional information about the state of the abdominal organs and blood vessels.

Treatment

Therapeutic and preventive measures in patients with cirrhosis begin with secondary prevention:

- prevention of infection with acute viral hepatitis, which, according to statistics, leads to the death of 50-60% of patients during the first year from the moment of its development;

- categorical refusal of alcohol, which can significantly improve the prognosis and life expectancy of patients;

- protection against hepatotoxic drugs.

Etiotropic therapy for most forms of cirrhosis is currently absent.

Assign a full-fledged balanced 5-6 meals a day for a better outflow of bile, regular stools (diet within table No. 5). With encephalopathy, protein intake is reduced to a level at which symptoms of ammonia intoxication do not appear. Table salt is limited, with ascites a salt-free diet is prescribed, supplementing the diet with foods rich in potassium. With itching and bradycardia, the volumes of meat proteins, legumes containing tryptophan, tyrosine, cystine and methionine, which are sources of toxic metabolites and ammonia, are reduced.

Patients in the inactive compensated stage of liver cirrhosis do not need drug therapy. They are periodically prescribed a complex of vitamins for oral administration.

With cirrhosis of the liver of moderate activity, to improve the metabolism of liver cells, preparations are recommended that include vitamins (vitamins B6 and B12, co-carboxylase, rutin, riboflavin, ascorbic acid, folic acid), lipoic acid, milk thistle extract. Courses of therapy are designed for 1-2 months. Herbal medicines are becoming increasingly important among this group of drugs. A purified dry extract obtained from the fruits of milk thistle, containing flavolignans and flavonoids, the drug Silimar has a pronounced hepatoprotective effect: it inhibits the growth of

indicator enzymes, stabilizing the cell membrane of hepatocytes, inhibits the processes of cytolysis, prevents the development of cholestasis. It exhibits antioxidant and radioprotective properties, enhances the detoxifying and exocrine function of the liver, has an antispasmodic and slight anti-inflammatory effect. The improvement of clinical manifestations in the form of a decrease in subjective complaints from patients, a decrease in biochemical indicators of the activity of the process in the liver has been reliably proven. According to the experiment, the following indicators were obtained: on the 7th day, the inhibition of the increase in activity for AST and ALT was 54.8%, on the 14th day - 66% of the initial background of ALT and a slightly smaller slowdown for AST, distinct (by 33-60%) dose-dependent decrease in GGT activity in blood serum. These changes were recorded in both acute and chronic experiments. The choleretic function of the drug was clearly observed at a minimum dosage of 50 mg per kg of body weight during 1 and 2 hours of the study and revealed its increase by 31.6% and 26.3%, respectively. Such indicators of the cholestasis syndrome as cholesterol, triglycerides, alkaline phosphatase completely returned to normal, and bilirubin and g-glutamine transpeptidase decreased to numbers exceeding the norm by 1.4 and 2.1 times, and initially they exceeded the norm by 3.1 and 5 ,4 times. In addition, in clinical trials, a clear normalization of gallbladder function was noted in patients with manifestations of hypomotor dyskinesia. It is these moments that make it possible to use Silimar in patients with liver damage against the background of cholestasis syndrome, in contrast to its analogues. The drug is used at any age with a course of 25 days to 1.5 months, 1-2 tablets 3 times a day 30 minutes before meals.

In the decompensated stage of liver cirrhosis with encephalopathy, ascites or severe hemorrhagic syndrome, the dose of lipoic acid or lipamide is increased to 2–3 g per day, the course of treatment is 60–90 days. Oral administration is combined with parenteral administration of drugs for 10-20 days. Essentiale is treated in the same way: inside 2-3 capsules 3 times a day and intravenously drip 10-20 ml 2-3 times a day in an isotonic solution. The course of combined treatment is from 3 weeks to 2 months. As the phenomena of hepatocellular insufficiency disappear, they switch to taking capsules inside. The total duration of the course of treatment is up to 6 months.

In viral cirrhosis of the liver of moderate activity with the presence of serum markers HBV, HCV, the use of prednisolone in a daily dose of 30 mg per day is indicated. Severe cytopenia is also an indication for the appointment. Gradually reduce the dose by 2.5 mg every 2 weeks. Maintenance dose - 15-7.5 mg is selected individually and taken for 2-3 years. A high degree of activity and a rapidly progressive course require high doses of the drug - from 40 to 60 mg. The use of corticosteroids in the decompensated stage of the disease is not indicated, as they contribute to the addition of infectious complications and sepsis, ulceration from the gastrointestinal tract, osteoporosis, catabolic reactions leading to renal failure and hepatic encephalopathy.

Treatment of patients with ascites is carried out by combining diuretic drugs: aldosterone antagonists and thiazide drugs. Combinations of spironolactone - ethacrynic acid, spironolactone - triampur, spironolactone - furosemide are effective. Daily urine output should not exceed 2.5-3 liters to avoid a noticeable imbalance of electrolytes. With the advent of powerful diuretics, paracentesis was practically stopped due to the loss of protein that occurs with it and the risk of infection.

There is no effective treatment for primary biliary cirrhosis. Corticosteroids do not significantly affect the course of the disease, but slow its progression. D-penicillamine suppresses the inflammatory reaction of the connective tissue, the development of fibrosis, reduces the content of immunoglobulins, the level of copper in hepatocytes. A noticeable effect is observed only with its long-term use (1.5–2 years). Ursodeoxycholic acid at a dose of 10–15 mg per kg of body weight for a period of 6 months to 2 years leads to an improvement in blood biochemical parameters with the disappearance of skin itching, weakness, and anorexia. Plasmapheresis brings temporary relief. Liver transplant is performed.

Indications for surgical treatment of cirrhosis are - severe portal hypertension with varicose veins of the esophagus in patients with bleeding, with varicose veins of the esophagus without bleeding; if a sharply dilated coronal vein of the stomach is detected in combination with high portal hypertension; hypersplenism with a history of esophageal bleeding or its threat. Various types of porto-caval anastomoses are used: mesenteric-caval, splenorenal, in combination with splenectomy or without it. Contraindications to surgical intervention are progressive jaundice and age over 55 years.

Forecast

Life expectancy over 5 years from the moment of diagnosis is observed in 60% of patients with alcoholic cirrhosis of the liver, in patients with viral cirrhosis - in 30%. In primary biliary cirrhosis, life expectancy is 5–15 years. The degree of compensation of the disease significantly affects the prognosis. Approximately half of patients with compensated cirrhosis live more than 7 years. With the development of ascites, only a quarter of patients survive 3 years. Even more unfavorable prognostic value is encephalopathy, in which patients in most cases die within the next year. The main causes of death are hepatic coma (40-60%) and bleeding from the upper gastrointestinal tract (20-40%), other causes are liver cancer, intercurrent infections, hepatorenal syndrome.

LITERATURE:

1. Юлдашова Ш. Т., Юлдашова Г. Т., Рахманова Н. Ж. Новейшие аспекты и бремя вирусного гепатита А. Предпосылки к вакцинам о профилактике в Республике Узбекистан //Современные технологии диагностики, лечения, профилактики инфекционных и паразитарных болезней. – 2019. – С. 90.

2. Юлдашева, Ш. (2021). Основные Тенденции Интегративно-Креативных Возможностей студентов в Высшем Медицинском учебном Заведении и их Влияние на их Деятельность. CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES, 2(3), 369-377.

3. Ergashevich N. F., Kholmurodovich U. F., Toyirovna Y. S. The effect of various hepatoprotectors on pathological syndromes in chronic liver diseases and determination of the specific gravity of drug groups //Middle European Scientific Bulletin. – 2020. – Т. 6. – С. 31-34.

4. Умаров Ф. Х., Нурбаев Ф. Э. Сравнительный ABS\VEN анализ лекарственных средств, используемых для лечение хронических гепатитов и цирроза печени в период 2006-2016 гг //Медицина и спорт. – 2019. – №. 2. – С. 46-49.

5. Умаров Ф. Х., Нурбаев Ф. Э. Фармако-экономический анализ расходов гапатопротекторов на лечение хронического гепатита в условиях стационара (ретроспективное исследование) //Медицина и спорт. – 2019. – №. 2. – С. 49-52.

6. Yuldashova Sh. T. Prerequisites for the Development of Creative Thinking // Middle european scientific bulletin // Volume 8, January 2021.-С. 287-289

7. Kholmurodovich U. F. Liver Fibrosis-Modern Methods of Diagnostics and Drug Correction //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2021. – Т. 2. – №. 2. – С. 158-167.

8. Kholmurodovich U. F. Damage to the digestive system when using non-steroidal anti-inflammatory drugs //European journal of modern medicine and practice. – 2022. – Т. 2. – №. 1. – С. 6-16.

9. Umarov, F. K. . (2022). The Effect of Pharmacological Agents on the Liver. Research Journal of Trauma and Disability Studies, 1(10), 4–16. Retrieved from http://journals.academiczone.net/index.php/rjtds/article/view/308

10/ Kholmurodovich U. F. Damage to the digestive system when using non-steroidal anti-inflammatory drugs //European journal of modern medicine and practice. – 2022. – Т. 2. – №. 1. – С. 6-16.

11. Kholmurodovich U. F. Liver Pathology In Rheumatoid Arthritis //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2022. – Т. 3. – №. 1. – С. 11-15.