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Diagnostic Significance of Hepatic Fibrosis in Patients with Extrahepatic Chronic Viral Hepatitis C

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Annotation: A retrospective analysis of 319 adult patients aged 18 to 71 years with CHC caused by HCV genotypes 1, 2, and 3 who were treated at the Bukhara IIB from 01/01/2018 to 11/30/2020 was carried out. The inclusion criteria for the study were serological confirmation of the presence of antibodies against CHC by ELISA, qualitative and quantitative determination of HCV RNA by polymerase chain reaction (PCR).

The results of liver elastography, the distribution of fibrotic processes in patients with chronic hepatitis C shows that the main group of patients with fibrotic processes of the F2-F3 stage was 74.1%, and in the control group of patients with F1-F2-stage fibrotic lesions - 63.8%. Fibrous lesions F0 - F1 stage in the main group was 21.4% of patients and in the control 47.9%.

Keywords: chronic hepatitis C, fibrascan, fibrosis, cryoglobulinemic vasculitis, elastography

Relevance of the topic

According to the World Health Organization, 3% of the world's population (about 170 million people) are infected with hepatitis C virus (HCV), while the disease in 85% of cases becomes a chronic process, ending in 15-25 years with cirrhosis or primary liver cancer [1].

Hepatotropic viruses primarily affect hepatocytes, and can cause extrahepatic manifestations with damage to other organs [2]. The decisive pathogenetic mechanism is caused by immune responses against viral pathogens with the deposition of immune complexes in target tissues. Extrahepatic manifestations of any form occur in 74% of patients with chronic HCV infection and overt hepatic disease emissions, manifested by non-specific health problems, including malaise, fatigue, nausea, weight loss, and musculoskeletal pain [3]. Extrahepatic manifestations include arthralgia, myalgia, and rash [4, 5]. Nevertheless, antiviral therapy is very effective in acute infection, leading to the disappearance of HCV with a sustained virological response [6]. Persistent HCV infection is the leading cause of chronic liver disease.

Although it is mostly treatable with direct-acting antiviral therapy (DAA), the diagnosis is made in only a subset of patients. Notably, extrahepatic manifestations occur in almost three fourths of victims with chronic HCV infection, with cryoglobulinemia being the most common manifestation (in 40–60% of infected patients) [7]. Clinical manifestations include arthralgia, myalgia, glomerulonephritis, Raynaud's phenomenon, Sjögren's syndrome, Hashimoto's thyroiditis, Graves' disease, ulcerative keratitis, peripheral neuropathy, and cryoglobulinemic vasculitis. Occasionally, extrahepatic comorbid autoimmune diseases, such as cryoglobulinemic vasculitis, may lead to the diagnosis of HCV infection. Long-term eradication of HCV with IFN-α or DAA has been shown to have a beneficial effect on outcomes after these manifestations [8]. Notably, a prospective study of 9895 HCV infections treated with DAAs found that viral clearance was responsible for the significant reduction in extrahepatic HCV mortality.

Under conditions of such diverse and dynamic processes, precise formulation is a serious problem. Histological analysis by liver biopsy, traditionally considered the gold standard, is not safe. Moreover, it is subject to both observer and sample bias, as well as significant variability. Over the past two decades, various non-invasive approaches for liver fibrosis staging have been proposed and evaluated, with sometimes conflicting reports on diagnostic accuracy and reproducibility. Certain technical and patient characteristics affect the performance of different tests differently, as well as specific patient groups with special considerations.

Rather, the identification of progressive fibrosis and cirrhosis may be much more important for comprehensive prevention and treatment strategies, as well as an individual approach to treatment.

The results of needle biopsy with histological examination of the material have been the “gold standard” for the diagnosis of fibrosis in chronic liver diseases (CKD) for decades [9]. Despite the high information content of the biopsy, this invasive procedure is not without drawbacks. The most important aspect of a liver biopsy is the risk of postoperative complications. Complications such as moderate to severe pain at the puncture site or periprocedural hypotension are considered minor and do not outweigh the benefit of a diagnostic intervention. The most common and serious complication is bleeding, which occurs in 0.1–4.6% of biopsies performed [10]. The availability and acceptance of non-invasive tests (NIT) including various biochemical serum markers as an alternative to biopsy for diagnosing advanced fibrosis and determining prognosis in CKD is currently growing [11,13]. Modern NITs do not have significant side effects and contraindications for sampling, however, as these tests are increasingly included in daily clinical practice, diagnostic limitations arise that must be taken into account when interpreting the results.

The most studied and widely used in clinical practice after biopsy is FibroTest, as it has the highest diagnostic accuracy [12,14, 15].

Purpose of the study. To study the clinical characteristics of chronic hepatitis C with extrahepatic manifestations and the assessment of the severity of liver fibrosis in patients with chronic viral hepatitis C with extrahepatic manifestations using the Fibroscan apparatus.

Materials and methods of research

A retrospective analysis of 319 adult patients aged 18 to 71 years with CHC caused by HCV genotypes 1, 2, 3 who were treated at the Bukhara IIB from 01/01/2018 to 11/30/2020 was carried out. The inclusion criteria for the study were serological confirmation of the presence of antibodies against CHC by ELISA, qualitative and quantitative determination of HCV RNA by polymerase chain reaction (PCR).

The etiological verification of hepatitis was carried out by serological methods with the detection of anti-

HCV-core, unprotected proteins NS3, NS4, NS5, PCR of the IQ5 CUCLER genotype from the moment of nucleic acid amplification. Complaints of patients, indicators of a general blood test, a biochemical blood test were studied: determination of the activity of aspartate aminotransferase (AST), alanine aminotransferase (ALAT), alkaline phosphatase (AP), bilirubin, cholesterol, total protein, protein fractions, creatinine, urea, glucose, C- reactive protein (CRP) in the blood serum, rheumatic factor, coagulogram parameters, cryoglobulins (CG) were determined in the blood, ultrasound data of the abdominal organs and elastography parameters were analyzed.

Results and discussion

For a more detailed analysis, all patients were divided into 2 groups. The first group consisted of patients with CG (total n=112 or 35.1%, mean age 57.8±15.6 years). The second group consisted of patients in whom CG was not detected in the blood (total n=207 or 64.9%, mean age 50.7±11.6 years). At the first stage, the frequency and spectrum of extrahepatic manifestations of HCV infection were studied. The incidence of cryoglobulinemia in the study population of patients with HCV infection was 35.1% (n=112), of which males - 53.6% (n=60) and females - 46.4% (n=52), (male/female ratio 1.2/1).

The most common extrahepatic manifestation of chronic HCV infection is depression. According to the results of our analysis, among CVHC patients, depression was observed in 33.0%. The development of type 2 diabetes mellitus is observed in 13.4% of patients with chronic hepatitis C.

Cryoglobulinemic vasculitis was observed in 34.8% (n=39) of cases, among its manifestations: arthritis 28.2% (n=11), hemorrhagic vasculitis 46.2% (n=18), peripheral neuropathy 15.4% (n=6) chronic glomerulonephritis 5.1% (n=2). 2 cases of B-cell lymphoma were registered in male patients at the stage of liver cirrhosis (mean age - 36.0 years) (Fig. 1.).

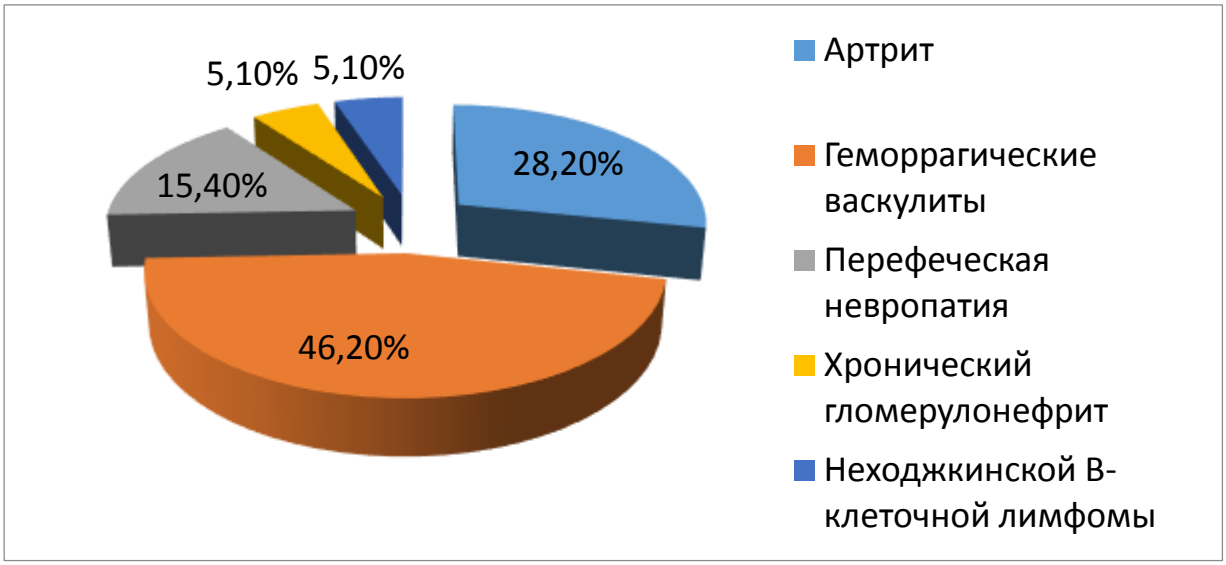

Fig. 1. The frequency of manifestations of cryoglobulinemic vasculitis

According to the results of liver elastography, the distribution of fibrotic processes in patients with chronic hepatitis C shows that the main group of patients with fibrotic processes of the F2-F3 stage was 74.1%, and in the control group of patients with the F1-F2 stage, fibrous lesions were 63.8%. Fibrous lesions F0 - F1 stage in the main group was in 21.4% of patients, and in the control group - 47.9% (Fig. 2.3).

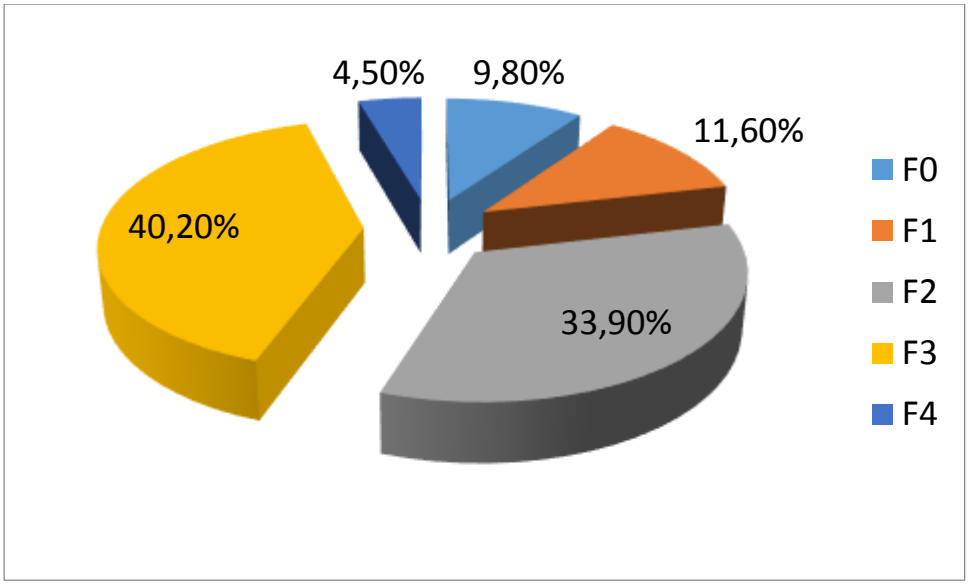

Fig. 2. Results of assessing the degree of fibrosis in patients of the main group

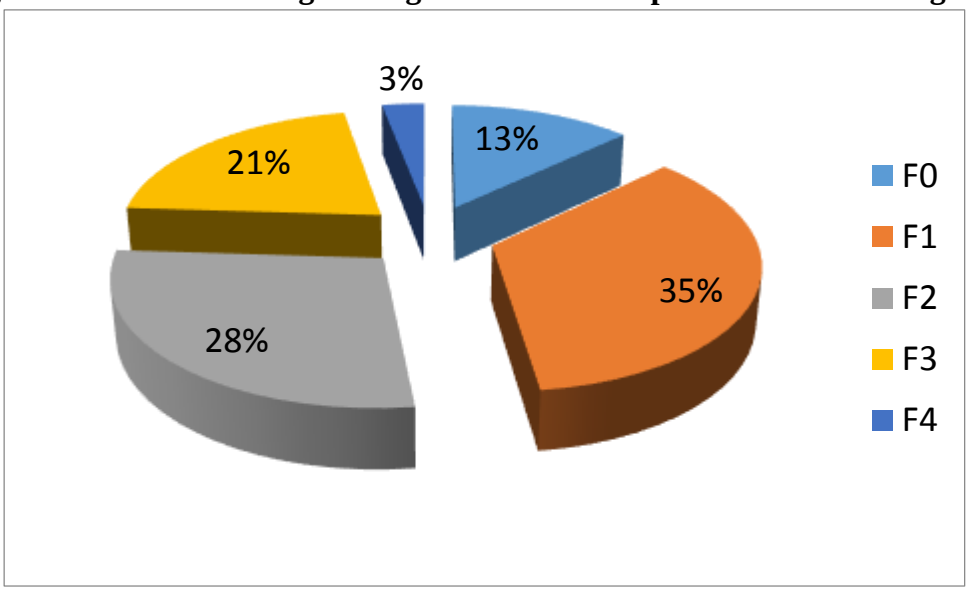

Fig. 3. Results of assessing the degree of fibrosis in patients of the control group

Table. Elastographic parameters of patients of the main and control groups.

Fibrosis stage	Average value, kPa		Interval of average values, kPa	
	Main group	Control group	Main group	Control group
F0	5,4	4,8	4,4-5,8	3,9-5,4
F1	6,9	6,2	5,9-7,1	4,8-6,5
F2	9,1	8,0	6,3-9,5	6,3-8,7
F3	11,9	10,8	10,1-14,5	8,8-13,5

Fibrosis stage	Average value, kPa		Interval of average values, kPa	
	Main group	Control group	Main group	Control group
F4	26,5	24,6	26,5-33,7	23,5-30,7

The elastographic parameters of the examined patients are presented in the table. The table data show that in patients of the main group of patients, F3 was mainly in the range of 10.1–14.5 kPa, while in the control group it was 8.8–13.5 kPa. The F4 level averaged 26.5 kPa in patients of the main group and 24.6 kPa in the control group ($P<0.001$).

Conclusion:

1. Liver elastometry can be used for non-invasive diagnosis of liver fibrosis in patients with chronic viral hepatitis C with extrahepatic manifestations.
2. The results of liver elastometry are very important criteria at all stages of development, which in turn allows us to compare their diagnostic accuracy with the results of a morphological study of liver tissue.
3. The impossibility of assessing the activity of hepatitis limits the use of elastometry only as an independent method for monitoring the development of liver fibrosis.

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