

FREQUENCY OF SYSTEMIC PATHOLOGY AT PATIENTS WITH HCV AND HBV – INFECTIONS

^aGAUHAR KURMANOVA, ^bNIGORA AKESHOVA

^a*Al-Farabi Kazakh National University 050040, 71 al-Farabi Ave., Almaty, Kazakhstan*

^b*H.A. Yassawi International Kazakh-Turkish University, 161200, 29 B.Sattarxanov Str., Turkistan, Kazakhstan*

email: ^agkurman@mail.ru, ^bnigora_akeshova@mail.ru

Abstract: Chronic Viral Hepatitis (CVH) is a widespread progressive liver disease. A viral hepatitis B and C cause development of cirrhosis and hepatocellular carcinoma. From 500 to 700 thousand people annually die due to HBV infection, and 350 thousand people die due to CVH all over the world. But mortality rate due to the systemic pathology associated with HCV and HBV is not considered to be a result of hepatitis C and B. The purpose of the article is to study frequency and nature of systemic comorbidity at patients with a chronic viral hepatitis B and C. The research is aimed to: find out what pathologies the patients with CVH the most often have; to know what disease was usually revealed at patients with HCV infection, and what diseases were the most often observed at patients regarding the hematopoietic system. Our main task is to reveal, study, and analyze the frequency of systemic pathology at patients with HCV and HBV – infections, compare them and then make the underlying conclusions. According to these conclusions, we will understand a full clinical presentation of the pathology.

Keywords: Chronic viral hepatitis B and C, digestive tract, cardiovascular and genitourinary system, diabetes mellitus, HCV, HBV, pathology.

1 Introduction

We began our research because hepatitis is one of the most dangerous diseases among people all over the world which cause death. We are going to make the research on this topic in order to observe, to know, reveal, analyze, learn, and understand the nature, mechanism, the main Factors, objects, reasons of systemic pathology, and namely two types of the disease (hepatitis B and C). We need to understand the pathology caused by hepatitis, and the process of the disease and its impact on the human body. Naturally, we have to find out the differences between the first and the second type. Then it is required to reveal the origins of hepatitis' occurring.

Hepatitis B and C are a very widespread and insidious disease which affects a very great number of people all over the world. That is one of the most harmful diseases that are often mortal. So, our research is very important for modern medical science, medicine, and should contribute to the improvement of diagnostics, prevention, treatment of two types of hepatitis.

In 57% of cases chronic viral hepatitis B and C cause the development of cirrhosis, in 78% of cases, they cause hepatocellular carcinoma (HCC). More than 500 thousand people annually die due to HBV infection, and more than 300 people die due to CVH C all over the world. (1) Chronic hepatitis C makes significant challenges for timely diagnosis and

treatment, as it is revealed occasionally during an examination in 70-80% of cases regarding other diseases or through contact with people sick with VH. (2)

In 15 -30% of cases CVH, in -25-50% of CVH C, in 70 -80% CVH D leads to cirrhosis, averagely 15-20% of patients have hepatocellular carcinoma based on cirrhosis. (3-5)

In some cases, diverse pathology of other organs and systems that defines the disease prognosis dominates along with hepatitis by itself. These signs may be independent pathology (regardless of the patient's chronic HCV or HBV infection) or may show the systemic nature of HCV or HBV infection. Immune reactions as a response to virus replication in the liver and beyond it are mainly important for the development of systemic pathology associated with HCV or HBV. (6-7)

According to comparative analysis of clinical, laboratory and immunological data people that with CVH may be divided into two groups: patients dominated by symptoms and syndromes caused by hepatic injuries; patients with system pathologic features of CVH, dominated by the symptoms which are not related to hepatic injuries (pathology of joints, neurological symptoms, hematological pathology, endocrinopathy, kidney and heart damages, etc.), but quite often specifically they determine the disease prognosis. (8-9)

In real clinical practice, it can be difficult to prove cause-and-effect link of HCV or HBV infection and pathology of organs and systems, which may be either a virus-associated or develop only independently. (10-11)

2 Materials and Methods

213213 patients with a Chronic Viral Hepatitis B and C were examined. The examination of patients with CVH was carried out according to the clinical protocol in 2 stages. ELISA diagnostics was carried out using test systems of CJSC Vektor-Best/Koltsovo, the Russian Federation. The polymerase chain reaction was carried out using the test systems and the equipment for PCR diagnostics (Litekh/Moscow). All the patients with CVH took genotyping by the PCR method. They took laboratory tools and techniques of a research according to the clinical protocol.

The work was carried out in the hepatological centre in Shymkent from 2014 to 2016. People sick with CVH were directed for examination from health care centres in Turkestan, Kentau, Taraz, Shymkent. The patients were examined and cured mainly on an outpatient basis. The data of 213 patients with CVH B and C were analyzed. Among the examinees, men were 50% (107), women – 50% (106) (Figure 1).

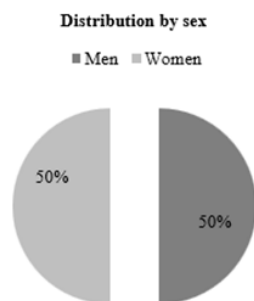


Figure 1. Distribution by Sex

The number of patients with CVH C and B of age 20-29 was 32 (15%), 30-39 – 68 (32%),

40-49 – 76 (36%), 50-59 – 28 (13%), 60-69 was 9 (4%) (Figure 2).

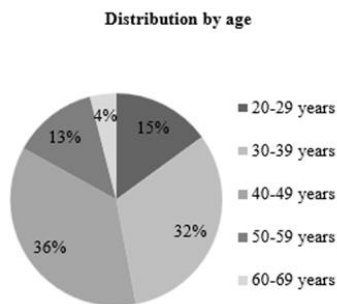


Figure 2. Distribution by Age

Examination of people with CVH was carried out according to the order of the Minister of Health of the Republic of Kazakhstan “On approval of the regulations to examine and cure patients with viral hepatitis” as of February 17, 2012 No. 92 in 2 stages. Stage 1: Serological examination. Diagnosis of HBV infection is approved by finding HBsAg and HBeAg in ELISA. When the antiHBe, antiHbcoreIgM and IgG are revealed, diagnosis is verified in PCR DNAHBV. Diagnosis of HCV infection was set on the basis of the revealed total anti-HCV and RNAHCV. If hepatitis B is revealed, the patients were examined for HDV infection using Elisa (anti-HDV) and PCR methods (HDVDNA). ELISA diagnostics was carried out using test systems of CJSC “VektorBest”/Koltsovo, the Russian Federation. The polymerase chain reaction was carried out using the test systems and the equipment for PCR

diagnostics (Litekh/Moscow). All the patients with CVH took genotyping by the PCR method. The researches using PCR and ELISA methods were carried out at LEGAL FIRM “CLINICAL AND DIAGNOSTIC LABORATORY OLYMPUS” LLC (the laboratory chief Gramotikopulo A. A.) at diagnostic center “INVIVO” LLC (the laboratory chief Popova M. A.). Among 213 examinees 77% (164) of them were with CVH C, 33% (49) – with CVH B. Only 9% (19) of patients had coinfection: 7% (15 patients) – CVH B + C, 2% (4 patients) – CVH B + D (Figure 3). During the analysis of the clinical signs, we compared a group of patients with HCV monoinfection and a group of patients with HBV infection mono along with HCV and HDV

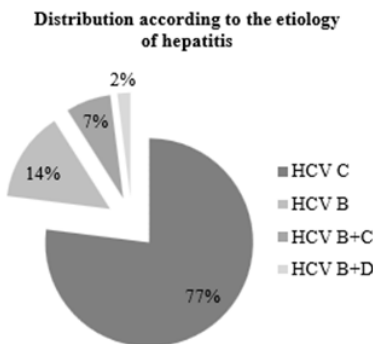


Figure 3. Distribution According to the Etiology of Hepatitis

When genotyping HCV are set as follows: genotype 1ab – 79 (48%) patients, 2a genotype – 23 (14%), genotype 3 ab – 52

(32%), and 10 (6%) patients whose genotype is not typed (Figure 4).

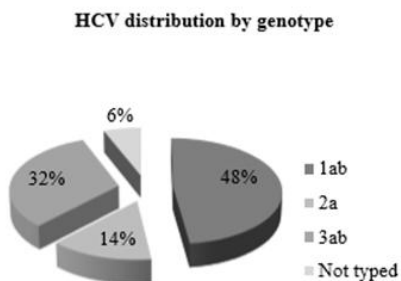


Figure 4. HCV Distribution by Genotype

To define the fibrosis level patients took liver elastometry using “FibroScan” device. Liver elastometry was carried out at the regional clinic in Shymkent. Among 213 examined patients 48

of them had F-0-1 that was relevant to 23% of patients, 71 (33%) had F-2, 66 (31%) had F-3, and 28 (13%) patients had F-4, which corresponds to cirrhosis (Figure 5).

Distribution according to the level of fibrosis

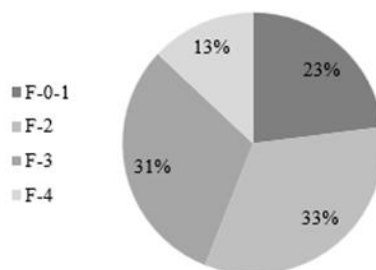


Figure 5. Distribution According to the Level of Fibrosis

Table 1 shows that among examinees 30 patients have CVH B monoinfection, 164 patients have CVH C, while the remainder is for mixed hepatitis. The average age of patients with CVH B is 35.9 ± 7.5 , while the average age of those with CVH C ranges from 36.3 ± 8.9 . Among examined patients with CVH B men suffer more frequently (59%) than women (41%), while with

CVH C women suffer more often (53%) than men (47%). According to the activity of infection process among patients with CVH B 25 (51%) patients had the minimal level of activity, 13 (27%) – low level, and 11 (22%) patients – moderate level (Figure 6).

Distribution of HBV by terms of activity

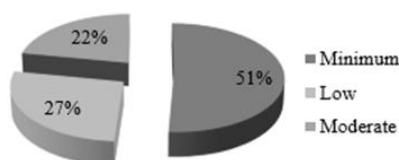


Figure 6. Distribution of HBV by Terms of Activity

Among the patients with CVH C 101 (62%) of them have a minimal level, 46 (28%) – low level and 17 (10%) – moderate

level of activity (Figure 7).

Distribution of HCV by terms of activity

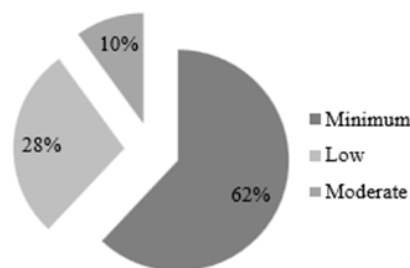


Figure 7. Distribution of HCV by Terms of Activity

Among the examined patients were those who had drug and alcohol addiction in their medical history. In the group of patients with CVH C, 6 patients have drug, and 7 of them have

alcohol addiction in their medical history. The same results were in the group of patients with CVH B: 7 patients have a drug addiction and 5 – alcoholism in their history.

Table 1. Features of Groups

	CVH B	CVH C	Total
Monoinfection	30	164	194
B+D	4		4
C+B		15	15
average age, in years	35.9 ± 7.5	36.3 ± 8.9	36.1 ± 8.2
of men	29	78	107
of women	20	86	106

minimal activity	25	101	126
low activity	13	46	59
moderate activity	11	17	28
drug addiction	7	6	13
alcohol addiction	5	7	12

Clinical examination of patients with HBV and HCV infections included detailed interview, defining of the epidemiological

history and anamnesis morbi (Table 2).

Table 2. Risk Factors for Infection of Viral Hepatitis

Epidemiological history	abs.	%
Acute Viral Hepatitis in history	36	16.9
visited the dental office	49	23
surgical and gynaecological interventions	33	15.5
contact inside family	18	8.4
sexual way	15	7
blood transfusion including plasma transfusion	15	7
injection drug use	13	6.1
medical manoeuvres at the hospital	11	5.2
professional contact of medical worker	11	5.2
possible prenatal infection	7	3.4
tattoo	5	2.3
Total:	213	100

The table shows that the most common risk factor for infections is treatment at the dentist (23% of cases), and various surgical gynecological interventions (15.5% of cases). Only in 17% of cases patients noted experienced acute viral hepatitis. Its etiological deciphering is either unknown or not record. Perinatal infection was supposed when viral hepatitis of the same etiology was revealed at the patient's mother. The clinical signs were seen at an early age.

According to the protocol all patients were treated by the following research methods:

- Specialist advice: gastroenterologist, neurologist, endocrinologist, cardiologist, therapist, infectiologist, hematologist, skin venereologist, allergologist;
- Ultrasound investigation of the liver, gall bladder, pancreas, and spleen;
- Esophagogastroduodenoscopy;
- Rheoencephalography, doppler sonography of brain vessels, brain computed tomography and MRI;
- Ultrasound investigation of the prehyoid gland;
- Definition of prehyoid gland hormones;
- Definition of glucose in blood;
- ECG, echo-cardiography. (12-14)

3 Results and Discussion

It was found out that patients with CVH B the most often had pathology of digestive tract, cardiovascular and genitourinary system. The most often diabetes mellitus was revealed at patients with HCV infection ($p < 0.01$) among comorbidity. The hypoplastic anemia (22% in case of HCV and 8.2% in case of HBV) and thrombocytopenia (22.1% and 10.2% respectively) were the most often observed at patients regarding the hematopoietic system.

According to instrumental methods of examination, the pathology from the digestive, urinary, cardiovascular, endocrine, reproductive, blood and autonomic nervous system were revealed at patients. (15-16)

According to a laboratory and instrumental examinations patients frequently had symptoms of gastritis, duodenitis, cholecystitis, and pancreatitis from the digestive system. Among the diseases of a digestive tract, a diagnosis of cholecystitis and pancreatitis is the most common. In the group of patients with CVH C 114 patients (69.5%) was diagnosed with cholecystitis as well as 42 patients (85.7%) ($R < 0.001$) in the group of CVH B. In

the first group of 85 patients (51.8%) with CVH C, and in the group 25 patients (51%) with CVH B pancreatitis was rarely seen. In 29.9% of cases (49 patients) patients with CVH C were diagnosed with gastritis. In 31.1% of cases (51 patients), they have verified the diagnosis of duodenitis. In the second group of patients with HBV infection 15 patients (30.6%) from 49 had gastritis. 17 patients (34.7%) had duodenitis.

According to an examination of ultrasound investigation, urinary tests and specialist advice pathologic features of the urinary system were revealed. Lithic diathesis was one of the kidney disorders. It was featured by high urates level in a simple urine test and equally often was seen in groups of patients with HCV and HBV infection. In 11% of cases (18 patients) people with CVH C and 10.2% of cases (5 patients) people with CVH B. Diagnosis of the urinary system, infection was set to 54 (32.9%) of 164 patients with HCV infection and 19 patients (38.8%) with the HBV.

According to the record of diagnosis and treatment of CVH all the patients had a cardiologist consultation. 42 patients were revealed to have arterial hypertension of different severity. 30 of 42 patients included the group of patients with CVH C. That was 18.3%. The other 12 patients (24.5%) suffered from CVH B. Also according to the ECG and thorough clinical interview patients were diagnosed with ischemic heart disease. Patients with CVH B had ischemic heart disease more frequently than patients with HCV infection. In 4.9 % of cases (8 patients) in the group of patients with CVH C, and in 18.4% of cases (9 patients) people with HBV ($R < 0.05$).

Among the patients with CVH disorder of the endocrine system was seen. That was clinically seen as diabetes mellitus, autoimmune thyroiditis, and Basedow's goiter. Female patients with CVH often suffered from mastopathy, adnexitis, disorders of the menstrual cycle, endometriosis, stillbirth, and miscarriage. Also, there were cases when women were diagnosed with natural sterility and various tumors in the female genital zone. (17-18)

The frequency of diabetes mellitus was a bit different among patients depending on viral hepatitis etiology. In the group with CVH C patients had diabetes 2 times more than groups with CVH B reliably $R < 0.01$. In 13.4% of cases (22 patients) people with HCV infection and 6.1 % of cases (3 patients) the people with CVH B.

Female patients with HCV and HBV with the same frequency had such co-morbidities as natural sterility, endometriosis and benign tumors in the female genital zone. In 4.3 % of cases (7 patients) people with CVH C and 4.1% of cases (2 patients) people with CVH B have endometriosis. In 1.8% of cases (3 patients) people with HCV had sterility. In 4.9 % of cases (8 patients) people had tumors. The same results were found among patients with CVH B (sterility – 2.0%, tumors – 4.1%). Patients with the HBV most often suffered from menstrual cycle disorders. 20 (12.2%) and 14 patients (28.6%) with the HBV ($P < 0.05$) in groups with CVH C had menstruation disorder.

According to the research, patients with HCV more often had adnexitis, mastopathy, and miscarriages. In 14% of cases (23 patients) people with CVH C and in 10.2% of cases (5 patients) people with the HBV were diagnosed with adnexitis. Patients with CVH C had mastopathy in 5.5% of cases (9 patients), and miscarriages in 9.1% of cases (15 patients). 2 % (1 patient) –

mastopathy, 6% (3 patients) – miscarriages. Patients with an HBV were diagnosed with them.

Males of both groups were diagnosed with prostatitis with the same frequency. 15 patients (9.1%) from the group with CVH C and 5 patients (10.2%) from the group with CVH B suffered from the disease.

The pathology of the hematopoietic system was also revealed during the examination. Patients with CVH C in 22 % of cases (36 patients) had thrombocytopenia. The latter was approved laboratorially as a decrease of blood plates within $113-140 \times 10^9/l$. Diagnosis “hemophthisis” was verified among 36 patients (22 % of cases) and described as a decrease of hemoglobin level from 85-118g/l. In the group of patients with CVH B, these indexes differ. Thrombocytopenia was diagnosed among 5 patients (10.2%) ($P < 0.05$), hemophthisis – among 4 patients (8.2%) ($P < 0.001$) (Table 3).

Table 3. Intercurrent/systemic diseases among patients with CVH

n = 213	CVH C		CVH B		P
	n = 164		n = 49		
Comorbidity	abs.	M ± m	abs.	M ± m	
Digestive system					
Gastritis	49	29.9 ± 3.6	15	30.6 ± 6.6	
duodenitis	51	31.1 ± 3.6	17	34.7 ± 6.8	
cholecystitis	114	69.5 ± 3.6	42	85.7 ± 5.0	<0.001
pancreatitis	85	51.8 ± 3.9	25	51.0 ± 7.1	
Urinary system					
Urinary system infections	54	32.9 ± 3.7	19	38.8 ± 7.0	
lithic diathesis	18	11.0 ± 2.4	5	10.2 ± 4.3	
Cardiovascular system					
arterial hypertension	30	18.3 ± 3.0	12	24.5 ± 6.1	
ischemic heart disease	8	4.9 ± 1.7	9	18.4 ± 5.5	<0.05
Endocrine system					
diabetes mellitus	22	13.4 ± 2.7	3	6.1 ± 3.4	<0.01
Reproductive system					
prostatitis	15	9.1 ± 2.3	5	10.2 ± 4.3	
menstrual cycle disorders.	20	12.2 ± 2.6	14	28.6 ± 6.5	<0.05
adnexitis	23	14.0 ± 2.7	5	10.2 ± 4.3	
benign tumors in female genital zone.	8	4.9 ± 1.7	2	4.1 ± 2.8	
endometriosis	7	4.3 ± 1.6	2	4.1 ± 2.8	
mastopathy	9	5.5 ± 1.8	1	2.0 ± 2.0	
natural sterility	3	1.8 ± 1.1	1	2.0 ± 2.0	
stillbirth, miscarriage	15	9.1 ± 2.3	3	6.1 ± 3.4	
Autonomic nervous system					
Vegetovascular dystonia	13	7.9 ± 2.1	3	6.1 ± 3.4	
Hematopoietic system					
hemophthisis	36	22.0 ± 3.2	4	8.2 ± 3.9	<0.001
thrombocytopenia	36	22.1 ± 3.2	5	10.2 ± 4.3	<0.05
Other					
systemic candidiasis	4	2.4 ± 1.2	1	2.0 ± 2.0	
lichen acuminatus	1	0.6 ± 0.6	1	2.0 ± 2.0	
herpes recidivicus	3	1.8 ± 1.1	1	2.0 ± 2.0	
hemorrhoid	5	3.0 ± 1.3	4	8.2 ± 3.9	
allergosis	25	15.2 ± 2.8	5	10.2 ± 4.3	

Patients with HVG provided objectively more complaints. These complaints were mainly the sign of as the novegetative syndrome and syndrome of gastric indigestion. Nature of complaint and objective examination data mainly indicate the development of diverse pathologies of the intestine organs among patients with CVH B that is more frequent compared to

the patients with CVH C: chronic gastritis, cholecystitis, pancreatitis. (19)

Often complaints regarding the pathology of the digestive tract are firstly responsible for a patient's visit to a doctor. Upon further examination, they are diagnosed with chronic HBV and/or HCV infection. Pathogenesis of gastrointestinal tract

disorder is not clear enough. Development of gastritis, duodenitis, pancreatitis may be due to any virus. Otherwise, this is a reactive state. (2,20)

Higher regular gastrointestinal pathology among patients with viral hepatitis is related to some factors. Development of gastritis, duodenitis, pancreatitis may be due to replication of the viruses B and C in the cells of the mucous membrane. However, such replication is probably less important. Apparently, the more frequent reason is dysfunctions related to the actual process of chronic liver pathology, a disorder of fine regulation of the digestive processes by "small" hormones and regulatory proteins such as cholecystokinin. (3,21-22)

In the case of CVH, there is a bile outflow due to the development of biliary dyskinesia. In the case of biliary dyskinesia on the hypotonic type, reactive cholecystitis proceeds with stratification of infection (due to development of stagnant processes). Biliary dyskinesia on hypertonic type provides an increase of ductus choledochus pressure which can lead to an outflow of pancreatic secretion. (23) So, biliar-dependent pancreatitis is formed. In the case of hepatoenteric circulation, disorder bile flows chaotically into the duodenum. That hinders digestion and absorption of fat and other substances of lipid nature, reduces the bactericidal activity of duodenal content, leads to microbial semination of duodenum, weakens growth and functioning of normal intestinal microflora. Affected by microflora, bile acids are subject to an early deconjugation. At the same time, the mucose membrane of the duodenum, small intestine, and colon are hurt. Reflux gastritis, duodenitis, enteritis, and colitis proceed. Besides, dysbacteriosis itself increases pressure in the duodenum (due to fermentation and gasification processes), and then the bile is flown into stomach along with following irritation of mucous membrane and the development of reflux gastritis. Thus, all the above mentioned processes are closely interrelated. (4,24)

Reasonably, more frequent development of digestive tract pathology (which is either concomitant or systemic sign of CVH) in case of HBV infection is most probably due to the fact that all the pathogenetic mechanisms that are important in the pathology of the tract (virus replication, dysfunctions, immunocomplex vasculitis) are more prominent with HVH B.

Pathology of the blood system is a special group in case of HCV and HBV infection. Chronic viral hepatitis is often accompanied by anaemic and thrombocytopenic syndromes. Nosological entities are a special group of HBV and HCV infection. Direct cytopathic effect of viruses and/or the following development of immune disorders is important in the pathogenesis of these nosological entities: anaemia, immune cytopenias, peripheral pancytopenia, thrombocytopenia. (25)

Changes in the structure and metabolism of peripheral blood erythrocytes are very important to cause disorder of red blood system in case of chronic viral hepatitis. They typically precede quantitative changes in red blood indexes and are an early index of an erythron to be involved in the pathological process.

Endocrine disorders typical for CVH: diabetes mellitus, menstrual cycle disorders, adnexitis, benign tumors of the female genital zone, endometriosis, mastopathy, natural sterility, stillbirth, miscarriage. The frequency to reveal diabetes mellitus type II reaches 15-20% among patients with HCV infection. It depends on a patient's sex, age and the stage of disease (cirrhosis). Besides, among diabetics is a higher frequency of HCV infection than among the population. Mechanisms to proceed diabetes type II in case of HCV infection are rather vague. But it is found that α glucose tolerance increases due to interferon therapy. Despite insulin resistance may proceed regardless of VHC, a great number of clinical and experimental researches suggest that VHC is important in its pathogenesis. This aspect is important because insulin resistance may not only accelerate the development of cirrhosis and hepatocellular carcinoma in the outcome of CVH C but also may reduce the response to antiviral therapy. (2,26-27)

The fact that VHC may cause diabetes mellitus was firstly supposed by Allison et.al. in 1994. Since that time dozens of research papers have been published to study the relationship between VHC and diabetes mellitus type II. Based on some researches carried out in various parts of the world we found that from 13% to 33% of patients with chronic CVH C more often have diabetes mellitus type 2. (3-4,28-29)

Adnexitis, benign tumors of female genital zones, endometriosis, mastopathy were the most common among patients with CVH C. (30) More frequent sign of hemorrhagic syndrome and dysmenorrhea among patients with hepatitis B also have to be explained. It should be noted that reproductive function disorder in case of HBV and HCV infections are due to the general vascular lesion. Immunocomplex vasculitis leads to degenerative changes in the pituitary-hypothalamic area, followed by the development of dysfunction in hormonal homeostasis.

Kidney damage with chronic infection due to HBV may be provided in multiple forms such as chronic glomerulonephritis, tubulo-interstitial nephritis, and nephropathy as part of vasculitis in case of giant cell arteriitis along with HBV infection. Pathogenesis of nephropathy associated with HBV is due to the formation of immune complexes which contain HBV antigens: HBsAg, HBeAg, HBeAg. (31-32)

Various viral agents of infections including those caused by hepatitis viruses are polysyndromes. Viruses are often considered to be etiological factors of myocarditis. Considering the clinically latent period of primary chronic forms of myocarditis we may suggest that in case of HCV infection myocarditis is far more seen than diagnosed. In the pathogenesis of myocardium disorder, the following things are discussed: the possibility of HCV replication in myocardium tissue, affect of cellular immunity responses on tissue virus antigens and autoantigens induced by it, and the role of immune complexes. The role of cytokines produced by immunocyte activated by the virus is discussed, which causes negative inotropism and lesion of the heart muscle through the mechanism of nitric oxide production increase.

Systematic destruction which may occur in the case of HCV and HBV infections shows the general nature of HBV infections involving many organs and tissues in the pathological process. That hinders early diagnostics and treatment of chronic hepatitis. A variety of system extrahepatic pathology which often exceeds the clinical presentation of hepatitis as a whole, taking a label of other disease and prevails over the moderate and low observed liver process for many years means that any specialist may meet chronic HCV and/or HBV infection and its outcomes. (33-34)

A systematic lesion which is observed in case of HCV and an HBV infection reflects the general nature of those viral infections involving many organs and tissues in the pathological process. Due to that early diagnostics and treatment of chronic hepatitis is complicated. That fact is to be considered by doctors of any qualification. Screening of HCV and HBV serum markers, as well as transaminases level, is appropriate at all patients with any chronic disease.

4 Conclusion

The reason to begin our research was the fact that chronic hepatitis is one of the most dangerous diseases among people all over the world which is often mortal. Nature, mechanism, the main factors, objects, reasons of systemic pathology, and namely two types of the disease (hepatitis B and C) were observed, known, revealed, analyzed, learned, and perceived. The pathology caused by hepatitis, the process of the disease and its impact on the human body are described in the article. The differences between the first and the second type were found out. The origins of hepatitis' occurring were revealed in the paper.

Hepatitis B and C affect a very great number of people all over the world. These diseases are ones of the most harmful diseases that often lead to death.

Cirrhosis occurs due to chronic viral hepatitis B and C in 57% of cases, whereas hepatocellular carcinoma – due to that in 78% of cases. The number of people who annually die due to HBV infection, and people dying due to CVH C at the global level is provided in our article. Significant problems for timely diagnosis and treatment of chronic hepatitis C are described.

The main idea of our article was implemented. We provided a definition of Chronic Viral Hepatitis, shown and researched the difference between hepatitis B and C, HBV infection and CVH C. We found out in what way Chronic Viral Hepatitis leads to systemic pathology, and how this pathology proceeds. The methods, laboratory tools and techniques to diagnose and reveal hepatitis B and C and systemic pathology were provided in the paper.

Literature:

- Zarski JP, Sturm, Guechot J, et al. Comparison of nine blood tests and transient elastography for liver fibrosis in chronic hepatitis C: the ANRS HCEP-23 study. *J Hepatol.* 2012 Jan.; 56(1):55-62.
- Thomson BJ, Finch RG. *Clin Microbiol and Infect.* 2005; 11(2):86-94.
- Boursier J, de Ledinghen V, Zarski JP, et al. Comparison of eight diagnostic algorithms for liver fibrosis in hepatitis C: New algorithms are more precise and entirely noninvasive. *Hepatology.* 2012 Jan; 55(1):58-67.
- EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. *Journal of Hepatology.* 2011; 55:245-64.
- Feldstein A, Kleiner D, Kravetz D, Buck M. Severe hepatocellular injury with apoptosis induced by a hepatitis C polymerase inhibitor. *J Clin Gastroenterol.* 2009; 43(374):81.
- EASL Clinical Practice Guidelines: management of chronic hepatitis B. European Association For The Study Of The Liver. *J Hepatol.* 2009 Feb; 50(2):227-42.
- Ghany M, Nelson D, Strader D, Thomas D, Seeff L. An Update on Treatment of Genotype 1 Chronic Hepatitis C Virus Infection: 2011. Practice Guideline by the American Association for the Study of Liver Diseases. *Hepatology.* 2011; 54(4):1433-44.
- Kohli A, Shaffer A, Sherman A, Kottlilil S. Treatment of hepatitis C: a systematic review. *JAMA.* 2014; 312:631-40. Available from: ncbi.nlm.nih.gov/pubmed/25117132
- Innes HA, McDonald SA, Dillon JF, et al. Toward a more complete understanding of the association between a hepatitis C sustained viral response and cause-specific outcomes. *Hepatology.* 2015; 62:355-64. Available from: ncbi.nlm.nih.gov/pubmed/25716707
- Hsu YC, Ho HJ, Huang YT, et al. Association between antiviral treatment and extrahepatic outcomes in patients with hepatitis C virus infection. *Gut.* 2015; 64:495–503. Available from: ncbi.nlm.nih.gov/pubmed/25398770
- Hsu YC, Lin JT, Ho HJ, et al. Antiviral treatment for hepatitis C virus infection is associated with improved renal and cardiovascular outcomes in diabetic patients. *Hepatology.* 2014; 59:1293–302. Available from: ncbi.nlm.nih.gov/pubmed/24122848
- Cacoub P, Gragnani L, Comarmond C, Zignego AL. Extrahepatic manifestations of chronic hepatitis C virus infection. *Dig Liver Dis.* 2014; 46(5):16573. Available from: ncbi.nlm.nih.gov/pubmed/25458776
- Sherman AC, Sherman KE. Extrahepatic manifestations of hepatitis C infection: navigating CHASM. *Curr HIV/AIDS Rep.* 2015; 12:35361. Available from: ncbi.nlm.nih.gov/pubmed/26208812
- Gragnani L, Fognani E, Piluso A, et al. Long-term effect of HCV eradication in patients with mixed cryoglobulinemia: a prospective, controlled, open-label, cohort study. *Hepatology.* 2015; 61:1145-53. Available from: ncbi.nlm.nih.gov/pubmed/25431357
- Gragnani L, FabbriZZi A, Triboli E, et al. Triple antiviral therapy in hepatitis C virus infection with or without mixed cryoglobulinaemia: a prospective, controlled pilot study. *Dig Liver Dis.* 2014; 46:833-7. Available from: ncbi.nlm.nih.gov/pubmed/26853322
- Saadoun D, Resche Rigon M, Pol S, et al. PegIFNalpha/ribavirin/protease inhibitor combination in severe hepatitis C virus-associated mixed cryoglobulinemia vasculitis. *J Hepatol.* 2015; 62:24-30. Available from: ncbi.nlm.nih.gov/pubmed/25135864
- Makara M, Sulyok M, Csacsovskzi O, Sulyok Z, Valyi-Nagy I. Successful treatment of HCV-associated cryoglobulinemia with ombitasvir/paritaprevir/ritonavir, dasabuvir and ribavirin: a case report. *J Clin Virol.* 2015; 72:66-8. Available from: ncbi.nlm.nih.gov/pubmed/26414149
- Gragnani L, Piluso A, Urraro T, et al. Virological and clinical response to interferon-free regimens in patients with HCV-related mixed cryoglobulinemia: preliminary results of a prospective pilot study. *Curr Drug Targets.* 2016. Available from: ncbi.nlm.nih.gov/pubmed/26853322
- Sise ME, Bloom AK, Wisocky J, et al. Treatment of hepatitis C virus-associated mixed cryoglobulinemia with direct-acting antiviral agents. *Hepatology.* 2016; 63:408-17. Available from: ncbi.nlm.nih.gov/pubmed/26474537
- Visentini M, Tinelli C, Colantuono S, et al. Efficacy of low-dose rituximab for the treatment of mixed cryoglobulinemia vasculitis: phase II clinical trial and systematic review. *Autoimmun Rev.* 2015; 14:889-96. Available from: ncbi.nlm.nih.gov/pubmed/26031898
- Arcaini L, Vallisa D, Rattotti S, et al. Antiviral treatment in patients with indolent B-cell lymphomas associated with HCV infection: a study of the Fondazione Italiana Linfomi. *Ann Oncol.* 2014; 25:1404-10. Available from: ncbi.nlm.nih.gov/pubmed/24799461
- Michot JM, Canioni D, Driss H, et al. Antiviral therapy is associated with a better survival in patients with hepatitis C virus and B-cell non-Hodgkin lymphomas, ANRS HC-13 lympho-C study. *Am J Hematol.* 2015; 90: 197-203. Available from: ncbi.nlm.nih.gov/pubmed/25417909
- Tasleem S, Sood GK. Hepatitis C associated B-cell Non-Hodgkin lymphoma: clinical features and the role of antiviral therapy. *J Clin Transl Hepatol.* 2015; 3:134-9. Available from: ncbi.nlm.nih.gov/pubmed/26357640
- Rossotti R, Travi G, Pazzi A, Baiguera C, Morra E, Puoti M. Rapid clearance of HCV-related splenic marginal zone lymphoma under an interferon-free, NS3/NS4A inhibitor-based treatment. A case report. *J Hepatol.* 2015; 62:234-7. Available from: ncbi.nlm.nih.gov/pubmed/25285757
- Romagnoli D, Marrazzo A, Ballestri S, Lonardo A, Bertolotti M. Sofosbuvir-based therapy cures hepatitis C virus infection after prior treatment failures in a patient with concurrent lymphoma. *J Clin Virol.* 2015; 69:74-7. Available from: ncbi.nlm.nih.gov/pubmed/26209383
- Sultanik P, Klotz C, Brault P, Pol S, Mallet V. Regression of an HCV-associated disseminated marginal zone lymphoma under IFN-free antiviral treatment. *Blood.* 2015; 125:244-67. Available from: ncbi.nlm.nih.gov/pubmed/25858892
- Lim LY, La D, Cserti-Gazdewich CM, Shah H. Lymphoma remission by interferon-free HCV eradication without chemotherapy. *ACG Case Rep J.* 2015; 3: 69–70. Available from: ncbi.nlm.nih.gov/pubmed/26504885
- Oliveira LP, de Jesus RP, Boulhosa RS, et al. Factors associated with insulin resistance in patients with chronic HCV genotype 1 infection without obesity or type 2 diabetes. *J Am Coll Nutr.* 2016; 2:1-7. Available from: ncbi.nlm.nih.gov/pubmed/26933768
- Younossi ZM, Stepanova M, Nader F, Younossi Z, Elsheikh E. Associations of chronic hepatitis C with metabolic and cardiac outcomes. *Aliment Pharmacol Ther.* 2013; 37:647-52. Available from: ncbi.nlm.nih.gov/pubmed/23384408
- Safi SZ, Shah H, Siok Yan GO, Qvist R. Insulin resistance provides the connection between hepatitis C virus and diabetes. *Hepat Mon.* 2015; 15:239-41. Available from: ncbi.nlm.nih.gov/pubmed/25741369
- Pavone P, Tieghi T, d'Ettorre G, et al. Rapid Decline of Fasting Glucose in HCV Diabetic Patients Treated with Direct Acting Antiviral Agents. *Clin Microbiol Infect.* 2016. Available from: ncbi.nlm.nih.gov/pubmed/26812446
- Morgello S, Murray J, Van Der Elst S, Byrd D. HCV, but not HIV, is a risk factor for cerebral small vessel disease. *Neuro*

Neuroimmunol Neuroinflammation. 2014; 1:27. Available from: [at ncbi.nlm.nih.gov/pubmed/25340079](http://ncbi.nlm.nih.gov/pubmed/25340079)

33. Lucchese A. A potential peptide pathway from viruses to oral lichen planus. J Med Virol. 2015; 87:1060-5. Available from: ncbi.nlm.nih.gov/pubmed/25776836

34. Blackard J T, Kong L, Huber A K, Tomer Y. Hepatitis C virus infection of a thyroid cell line: implications for pathogenesis of hepatitis C virus and thyroiditis. Thyroid. 2013; 23:863-70. Available from: ncbi.nlm.nih.gov/pubmed/23259732

35. Zeni LP, Viera PD, Michalczuk MT, Birkhan OA, Vilela MA, Alvares-da-Silva MR. Hepatitis C virus induces abnormalities in surface and intraocular pressure: a comparative study. Eur J Gastroenterol Hepatol. 2013; 25:411-5. Available from: ncbi.nlm.nih.gov/pubmed/23470265.

Primary Paper Section: D

Secondary Paper Section: DJ