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Clinical Course and Outcome of Acute Hepatitis E Infection in Patients with Chronic Hepatitis B and C

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Abstract

Hepatitis E virus (HEV) is the most common cause of enteral non-A, non-B hepatitis. Alcohol abuse, concomitant liver diseases and immunosuppression are thought to increase the risk of contagion, severe illness, and development of chronic disease. HEV infection might take a severe course in those coinfected with other hepatotropic viruses.

Objectives: The aim of this paper is to present a retrospective analysis of the clinical course and outcome of acute hepatitis E infection in patients with confirmed chronic hepatitis B and C infection, who were treated at the Department of Infectious Diseases of Pazardzhik Multiprofile Hospital for Active Treatment, Pazardzhik, Bulgaria between 2013–2017.

Materials and Methods: 25 patients, 22 males and 3 females, with acute hepatitis E infection and concomitant chronic hepatitis B and C infection. The methods used include epidemiological study, clinical observation, laboratory, and serological tests for detection of viral antigens and antibodies, and medical imaging (abdominal ultrasonography). The diagnosis of acute hepatitis E was established by the detection of specific anti-HEV IgM, IgG antibodies in significantly high values; chronic HBV and HCV infection was confirmed by the detection of viral antigens and specific antibodies.

Results: Chronic HBV infection was found in 18 of the patients (72%), 6/25 (24%) were with chronic hepatitis C, whereas only 1 (4%) had chronic HBV/HCV coinfection. 40% had cardiovascular disease and/or diabetes, 7 had cirrhosis. Alcohol abuse was reported by 7 patients. Complication due to acute on chronic liver failure was observed in 4 patients, 2 of whom died. The disease end in recovery in 23 patients.

Conclusion: People with pre-existing liver diseases, including chronic viral hepatitis, are at increased risk of severe hepatitis E and unfavorable outcome. Further studies among larger group that include people from risk groups and the general population would contribute to the better understanding of hepatitis E infection.

Introduction

Hepatitis E virus (HEV) is the most common cause of enteral non-A, non-B hepatitis [1, 2]. It is usually transmitted via fecal-oral route by the consummation of contaminated water and meat products. Transmission is also possible by transfusion of blood product from infected donors, as well as during birth from an infected mother [2–4].

In the endemic regions in Middle Asia and Africa, hepatitis E virus causes water outbreaks, while sporadic cases of HEV infection are observed in the industrialized countries due to the consumption of undercooked meat and meat products [3, 4].

People with underlying liver diseases, alcohol abusers and immunocompromised ones are at increased risk of getting infected with HEV, experiencing a severe disease, and developing chronic infection. Recently, it has been observed an increase in the anti-HEV IgG seroprevalence among the general population and people of different risk groups [1, 2, 4–6].

HEV infection might take a severe course in those coinfected with other hepatotropic viruses. An exacerbation of chronic HBV infection has been documented in patient with acute hepatitis E [7–9].

In view of this, we herein present a retrospective study on the clinical course and the outcome in patients coinfected with HEV, HBV and HCV.

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Materials and Methods: 25 patients, 22 males and 3 females, with acute hepatitis E infection and concomitant chronic hepatitis B and C infection. The methods used include epidemiological study, clinical observation, laboratory, and serological tests for detection of viral antigens and antibodies, and medical imaging (abdominal ultrasonography). The diagnosis of acute hepatitis E was established by the detection of specific anti-HEV IgM, IgG antibodies in significantly high values; the diagnosis of chronic HBV and HCV infection was confirmed by the detection of viral antigens and specific antibodies.

Results: Patients were classified according to the underlying chronic hepatitis, comorbidities, and risk factors.

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Chronic HBV infection was found in 18 patients (72%), 6/25 (24%) were with chronic hepatitis C, whereas only 1 (4%) had chronic HBV/HCV coinfection. Fifteen patients (60%) had no comorbidities, however, 10/25 (40%) had accompanying disease – 3 patients reported cardiovascular diseases, 2 had diabetes and 5 had both cardiovascular diseases and diabetes. Underlying cirrhosis was found in 7 patients (28%) and all of them reported long-term excessive alcohol consumption. Only 1 patient had used intravenous drugs (Table 1).

Adynamia was the most common symptom, whereas only 2 patients complained of fever (up to 38°C) and arthralgia. Nineteen patients (76%) had jaundice, 6 patients were anicteric on admission, however, 1 of them developed icterus during the hospital stay. Most of the patients (22/25, 88%) had more than one symptom and the other 3 experienced only adynamia (Table 2).

Physical examination revealed hepatomegaly in 21 (84%) and hepatosplenomegaly was found in 4 (16%). One man with concomitant cirrhosis had also presented with telangiectasia on the trunk and rectal bleeding.

All patients underwent an abdominal ultrasonography that confirmed the physical findings. The abdominal ultrasound examination detected ascites in 4 of the patients, calculous chronic cholecystitis in 3, and steatosis in 5.

In most of the patients the highest values of total bilirubin and ALT were detected on the admission. One of the anicteric patients developed icterus after the admission – the total bilirubin reached 206 μmol/l, whereas ALT slightly increased reaching a highest value of 400 IU/l. This patient was with concomitant cirrhosis and developed acute liver failure, hepato-renal syndrome and gastrointestinal bleeding also occurred (Table 3).

Nearly half of the patient underwent a hospital treatment between one and two weeks. The shortest inpatient period was 7 days and the longest – more than a month (Table 4).

Severe thrombocytopenia was observed as a complication in two patients. One of them was with manifested rectal bleeding. With the improvement of the general condition, the platelets count came to normal.

On discharge, all patients were anicteric with reduced values of the liver enzyme and in improved general condition. The disease end in recovery in 23 of the patients after a convalescent period of about 30 days.

Two of the patients with underlying liver cirrhosis died due to the development of acute liver failure, haemorrhagic complication, ascites, and oedematous syndrome with subsequent pulmonary and cerebral oedema. The total bilirubin in one of these patients reached 600 μmol/l

The two patients who were treated more than a month spent in hospital 41 and 39 days respectively. They also had underlying cirrhosis and experienced a severe disease with decompensation of the liver functions. Treatment resulted in compensation of the complications and subsequent improvement of the general state. After the discharge the patients were sent to gastroenterologist for further observation and treatment.

Discussion and Conclusion

Hepatitis E infection is usually asymptomatic. The seroprevalence among people of the endemic regions, who have not experienced symptoms of hepatitis E, varies between 30 – 80%. Around 5 – 30 % of the infected ones develop acute icteric hepatitis that usually has a self-limiting course [10–12].

Hepatitis E might take a severe course in persons with pre-existing liver disease, including ones who persistently consume excessive amount of alcohol [13, 14].

All the patients presented in this paper manifested with symptoms and signs of hepatitis, and all of them were with concomitant chronic hepatitis B or/and C. Four of the patients, had underlying liver cirrhosis due

Table 1: Concomitant conditions, comorbidities, and risk factor.

	Chronic hepatitis			Comorbidities			Cirrhosis	Abuse	
	HBV infection	HCV infection	HBV+HCV infection	CVD	Diabetes	CVD and diabetes		Alcohol	Drugs
N (%)	18	6	1	3	2	5	7	7	1
	72%	24%	4%						
Total	25 (100%)			10 (40%)			7 (28%)	7(28%)	1 (4%)

HBV – Hepatitis B virus; HCV – hepatitis C virus; CVD – cardiovascular diseases

Table 2: Patients' symptoms and sign on admission.

	Dyspeptic complaints	Adynamia	Jaundice	>1 symptoms	Hepatomegaly	Hepatosplenomegaly
N (%)	19 (76%)	20 (80%)	19 (76%)	22 (88%)	21 (84%)	4 (16%)

Table 3: Laboratory values of total bilirubin and ALT on admission.

	Total bilirubin, μmol/l				ALT, IU/l			
	<35	35 ÷ 100	100 ÷ 200	>200	50 ÷ 500	500 ÷ 2000	2000 ÷ 3000	>3000
N (%)	6 (24%)	7 (28%)	5 (20%)	7 (28%)	7 (28%)	13 (52%)	4 (16%)	1 (4%)

Table 4: Duration of hospital stay and disease outcome.

	Duration of hospital stay				Outcome	
	7 days	7 ÷ 14	15 ÷ 30	>30	Recovery	Death
N (%)	3 (12%)	12 (48%)	8 (32%)	2 (8%)	23 (92%)	2 (8%)

to chronic hepatitis B or C infection and excessive alcohol consumption. These patients develop acute liver decompensation with subsequent life-threatening complications and, unfortunately, two of them died.

It had been documented that patients with underlying liver impairment might experience severe hepatitis E infection with the development of acute on chronic liver failure [13, 14].

In India the lethality rate of HEV infection in people with pre-existing liver disease reaches 70% [14–16]. The data from the industrialized countries are quite similar [17].

According to published data from endemic and nonendemic regions, anti-HEV seroprevalence among alcohol abusers is significantly higher [5, 6]. Similar tendency has been found in an observation from Pazardzhik, Bulgaria, published in 2022 [18].

A study from the United States between 2011 – 2018 among people with underlying liver disease (including alcohol-related liver injury, steatosis, chronic hepatitis B and C, autoimmune liver diseases and liver cirrhosis) estimates anti-HEV seroprevalence to be on the rise [19] and the data from Europe are analogical [1, 3, 5, 18, 20, 21]. Authors from Albania suggest a correlation between the seroprevalence and the stage of liver injury [22].

Hepatitis E has become a health issue of global concern that should be thoroughly investigated, especially among the risk groups. Little is known about the distribution of hepatitis E infection in Bulgaria and the clinical course of the disease among people with underlying comorbidities that are considered risk factors for severe disease and unfavorable outcome. Further studies among larger group that include people from risk groups and the general population would contribute to the better understanding of hepatitis E infection.

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