Int J Clin Exp Med 2015;8(9):16652-16657
www.ijcem.com /ISSN:1940-5901/IJCEM0010194

Original Article

Recent epidemiological and clinical features of acute hepatitis B in a single center of China

Xiaohong Chen*, Chengtao Fu*, Jia Liu, Lei Shan, Chenglin Liu

*Department of Infectious Diseases, The First Affiliated Hospital of Harbin Medical University, Harbin 150001, China. *Co-first authors.*

Received May 13, 2015; Accepted July 3, 2015; Epub September 15, 2015; Published September 30, 2015

Abstract: Aim: This study was to investigate the epidemiological and clinical features of acute hepatitis B. Methods: A retrospective study of 177 acute hepatitis B patients with an average age of 36.03 years and range of 7-62 years was conducted from Jan 2005 to Feb 2011. The epidemiological and clinical parameters were investigated. The serological markers and biochemical tests were examined. Results: 76.84% (n = 136) patients were icteric type, while 23.16% (n = 41) were non-icteric type. Other clinical manifestations for acute hepatitis patients included fatigue (82.49%), gastrointestinal symptoms (66.10%), yellowish discoloration of skin and sclera, fever (31.07%), rash 10 (5.65%), joint pain (2.82%) and headache (1.69%). One case presented with acute renal failure associated with acute hepatitis B. Nine cases suffered from fulminant hepatitis. After treatment, hepatic function was significantly improved ($P < 0.05$). For serological markers, 54 (30.51%) and 119 (67.23%) patients had HBsAg and HBV-DNA seroconversion respectively. Four deaths occurred due to the severe complications associated by acute infection of HBV during half a year period follow up. Conclusions: Adult males with occupation of workers and farmers are the high-risk population of acute hepatitis B in China. Several complications associated with acute hepatitis B should be noticed.

Keywords: Acute hepatitis B, epidemiology, clinical features, complications

Introduction

Hepatitis B virus (HBV), a DNA virus belonging to the virus family Hepadnaviridae, is transmitted through blood and sex contact [1]. The only known natural host of HBV is human [1]. HBV infection may lead to asymptomatic infection, acute self-limited hepatitis, fulminant hepatitis or chronic HBV infection [2]. Chronic HBV infection can lead to cirrhosis or hepatocellular carcinoma [3]. According to recent estimation of the World Health Organization, HBV is responsible for 500,000-700,000 deaths each year worldwide, most of which attribute to the chronic sequelae of HBV infection [4]. Most patients with acute self-limited hepatitis can recover from resolved infection in six months [1], and resolved acute infection is not considered a risk factor for cirrhosis or hepatocellular carcinoma [5]. In addition, owing to a number of public health intervention such as vaccination of infants and adolescents, the morbidity of acute hepatitis B has declined substantially worldwide [6, 7]. However, the incidence for HBV infection is still high and nearly 10% of patients with acute hepatitis B would develop into chronic hepatitis B [8]. In addition, acute HBV infection can also cause fulminant hepatitis, which is life-threatening [9]. Therefore, the prevention and treatment of acute hepatitis B should also be highly valued.

Over the past decade epidemiological and clinical characteristics of hepatitis B have changed, as described previously [10, 11]. In addition, new complication such as acute renal failure has been reported in patient with acute non-fulminant hepatitis B [12]. However, few studies were conducted on epidemiological and clinical characteristics among Chinese patients with acute hepatitis B. Thus, in order to better understand the etiology of acute hepatitis B and prevent it from transforming into chronic hepatitis B, meanwhile avoid the occurrence of life-threatening complications, we retrospectively investigated the epidemiological and clinical

Table 1. Epidemiological characteristics of the patients

Items	Number	Percentage (%)
Age (years)		
< 10	1	0.56
10-19	8	4.52
20-29	55	31.07
30-39	49	27.86
40-49	42	23.73
50-59	18	10.17
> 60	4	2.27
Gender		
Male	132	74.58
Female	45	25.42
Occupation		
Worker	59	33.33
Farmer	48	27.12
Staff	19	10.73
Student	7	3.95
Self-employer	16	9.04
Others	28	15.83
Transmission route		
Close contact	13	7.34
Frequently-eating outside	14	7.91
Blood transfusion	2	1.13
Dental work	3	1.69
Sexual transmission	1	0.57
Unknown	144	81.36
Onset season		
Spring	43	24.29
Summer	54	30.51
Autumn	44	24.86
Winter	35	20.34

characteristics as well as the treatment outcomes of acute hepatitis B.

Patients and methods

Patients

The present retrospective study was carried out in the department of Infectious Diseases of the First Affiliated Hospital of Harbin Medical University in China. A total of 177 patients with average age of 36.03 ± 11.2 years diagnosed with acute hepatitis B were included in this study between Jan 2005 and Feb 2011. Acute hepatitis B was diagnosed according to the viral hepatitis prevention and treatment programs made by the infectious and parasitic diseases sub-committee and the liver diseases sub-committee of Chinese Medical Association in 2000 and consisted of all of the following: 1) without a history of hepatitis B; 2) infection of hepatitis B virus (HBV) within the last six months; 3) signs and symptoms of acute hepatitis; 4) peripheral blood HBsAg positive; 5) HBV-DNA or anti-HBc-IgM positive in laboratory examinations.

For experiments involving human subjects, approval was obtained from the institutional review board of the hospital committee and the study was performed according to the Declaration of Helsinki.

Measurement of epidemiological and clinical characteristics

In the present study, the basic epidemiological information of recruited patients including age, gender, occupation, route of transmission and onset seasons were recorded. Moreover, clinical information of patients such as clinical manifestations, complications, interval time between disease onset and confirmed diagnosis, and hospital stays were also collected in the present study.

Laboratory tests

Acute phase serum was obtained from patient immediately after admission and thereafter at weekly intervals. Quantity testing of hepatitis B virus serologic marker (HBVM) was performed by enzyme-linked immunosorbent assay (Kehua Bio-engineering Co., Ltd, Shanghai, China). Serum alanine transaminase (ALT), aspartate aminotransferase (AST), albumin (ALB) and total bilirubin (TBIL) were detected using an automatic biochemical detector Olympus AU 5400 (Olympus Corporation, Tokyo, Japan). In addition, quantitative analysis of HBV DNA was performed by real-time fluorescence quantitative PCR (Kehua Bio-engineering Co., Ltd, Shanghai, China).

Treatment and follow-up

All the patients were given hepatoprotective and anti-inflammatory treatment. In addition, supportive and symptomatic therapies were also performed following the different clinical manifestation of different patients during hospitalization. Thereunto, 35 patients (19.77%) were given antiviral and immunomodulatory

Table 2. Clinical characteristics of the patients

Items	Number	Percentage (%)
Manifestations		
Fever	55	31.07
Fatigue	146	82.49
Yellowing of skin and sclera	136	76.84
Gastrointestinal symptoms	117	66.10
Rash	10	5.65
Joint pain	5	2.82
Headache	3	1.69
Oliguria and anuria	1	0.56
Complications		
Cholecystitis	31	17.51
Lung infection	15	8.47
Upper gastrointestinal bleeding	4	2.26
Abdominal infection	2	1.13
Bacteremia	1	0.56
Misdiagnosis	8	4.52
Type		
Icteric	136	76.84
Non-icteric	41	23.16

treatment, among which 9 cases were given nucleoside analogue treatment, 7 cases were given interferon, and 19 cases were given immunomodulators. Furthermore, patients were followed up for half a year after discharge.

Statistical analysis

Data were analyzed using SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA). The data were presented as mean ± standard deviation (S.D.). The comparisons before and after treatment were performed with paired t test, and $P < 0.05$ was considered statistically significant.

Results

Epidemiological characteristics

The epidemiological characteristics of patients with hepatitis B were shown in **Table 1**. According to the age, patients were divided into seven groups: < 10 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years and > 60 years. Following the results, hepatitis B occurred most commonly among young patients between 20 and 49 years accounting for 82.66% of all patients and the highest rate of acute hepatitis B was among patients at the age of 20 to 29 (31.07%). In addition, male patients seemed more susceptible to HBV than females in the present study (male *vs.* female = 74.58% *vs.* 25.42%). Considering occupation distribution, workers and farmers were the high-risk groups for acute hepatitis B accounting for 33.33% and 27.12% of all patients, respectively. Patients with definite infection routes of HBV occupied 18.64% of all the patients, and patients having a close contact with patients with hepatitisB or HBV carriers and often eating out had a high risk for acute hepatitis B. However, most patients with unknown infection route occupied vast majority (81.36%) of all patients. Furthermore, the onset season of 30.51% patients was in summer, which is the highest rate among four seasons with 24.86% in autumn, 24.29% in the spring and 20.34% in the winter.

Clinical characteristics

The clinical information of included patients was recorded in **Table 2**. There were 136 cases (76.84%) with icteric hepatitis and 41 cases 23.16% with non-icteric hepatitis. We also recorded the clinical manifestations of included patients. A large proportion of patients showed fatigue (82.49%), the yellowing of skin and sclera (76.84%) and gastrointestinal symptoms (66.10%). Other clinical manifestations of patients with acute hepatitis B included fever (31.07%), rash (5.65%), joint pain (2.82%) and headache (1.69%). Moreover, one patient presented oliguria and anuria. In addition, patients with acute-onset accounted for 99.44% (176/177), and one patient (0.56%) was diagnosed with acute hepatitis B during physical examination.

Several complications were reported in 53 patients including cholecystitis in 31 patients (17.51%), lung infection in 15 patients (8.47%), upper gastrointestinal bleeding in 4 patients (2.26%), abdominal infection in 2 patients (1.13%) and bacteremia in one case (0.56%). In addition, eight patients has experienced a history of misdiagnosis, with four patients (2.26%) misdiagnosed with chronic hepatitis B, one patient (0.56%) with fever of unknown origin, one patient (0.56%) with diabetic ketoacidosis, and the rest one (0.56%) with polymyositis (**Table 2**).

Thirty-one patients had been definitely diagnosed with acute hepatitis B in the local hospitals before admission to our hospital. Most of the remaining patients were diagnosed in a

Table 3. The improvement of hepatic function after treatment during hospitalization

Items	Admission	Discharge	*P*-value
ALT (U/L)	1253.67 ± 1092.89	105.69 ± 146.58	< 0.05
AST (U/L)	851.26 ± 1111.88	54.04 ± 59.94	< 0.05
ALB (g/L)	39.89 ± 5.23	43.34 ± 28.81	> 0.05
TBIL (μmol/L)	177.61 ± 171.79	62.57 ± 97.85	< 0.05

ALT, alanine transaminase; AST, aspartate aminotransferase; ALB, albumin; TBIL, total bilibrubin.

timely manner after the onset of the disease. The average interval time between disease onset and confirmed diagnosis was 12.02 ± 8.571 days, with the range of 3-61 days. The average hospital stay of patients was 22.33 ± 14.48 days, ranging from 1-110 days.

Changes of hepatic function after treatment

The changes of hepatic function were shown in **Table 3**. There was an obvious improvement of the hepatic function of the patients after comprehensive treatment. Significant decrease of ALT (before *vs.* after: 1253.67 ± 1092.89 *vs.* 105.69 ± 146.58, $P < 0.05$), AST (before *vs.* after: 851.26 ± 1111.88 *vs.* 54.04 ± 59.94, $P < 0.05$) and TBIL level (before *vs.* after: 177.61 ± 171.79 *vs.* 62.57 ± 97.85, $P < 0.05$) was observed among patients.

Treatment outcomes and follow up

After discharge, patients were followed up with a period of half of a year. There were 107 patients (60.45%) considered clinically cured and 59 cases (33.33%) were obviously improved, while four cases died and seven cases were lost to follow-up. In addition, all patients having accepted antiviral treatment were improved. Among 177 patients, nine cases (5.08%) suffered from fulminant hepatitis and symptoms were relieved in three cases after administration of antiviral nucleoside analogues (two patients took lamivudine and one patient took entecavir). Among the other six patients who were not given antiviral treatment due to undetectable HBV DNA, symptoms was relieved in one case, three patients died, and the other two patients were lost to follow-up.

We also recorded the changes of HBV during admission and follow up. Among 177 patients, 18 cases (10.17%) had HBsAg seroconversion and 51 (28.81%) cases had HBV-DNA seroconversion on admission, while these numbers had added to 54 (30.51%) and 119 (67.23%), respectively when they were discharged from our hospital. A total of 119 patients were detected the changes of HBV during the half-year follow up, 110 patients had HBsAg seroconversion and 114 cases had HBV-DNA seroconversion. Nine HBsAg positive cases had become chronic hepatitis B.

Discussion

Acute hepatitis B is a self-limited disease and most acute hepatitis patient patients would recover in six month after HBV infection [1]. However, there are still several cases that would develop into chronic hepatitis B, and several severe complications also have been reported on patients with acute hepatitis B [12, 13]. Several studies have been conducted to investigate the etiology and clinical features of acute hepatitis B from several countries except for China [11, 14, 15]. So we performed the present study to investigate the recent epidemiological and clinical features of patients with acute hepatitis B in a single center in China.

Demographic characteristic of included patients with acute hepatitis B indicated that male young patients accounted for the most proportion and the majority of them were workers and farmers. This part of the crowd accounts for a large number of population in China and has great fluidity. They have more opportunities to meet with various population including persons with chronic HBV infection, which are the major reservoirs for transmission [16]. HBV is transmitted by percutaneous or mucosal exposure to infected blood or other body fluid. HBV transmission occurred in various forms of human contact including mother-to-child; household (nonsexual); sexual; needle-sharing; and occupational/health-care-related [17]. We also reported the transmission routes of HBV in the present study. However, the transmission routes of a majority of patients could not be identified. We speculated that lots of patients concealed the facts or ignored some details in their daily life, while such large number of cases with unknown transmission routes still challenges the prevention of acute hepatitis B.

As previously described, patients with acute hepatitis B presents symptoms such as nausea, abdominal pain, fever, jaundice, vomiting and hepatomegaly or splenomegaly [1, 18].

In the present study, 76.8% cases were with icteric hepatitis. The other clinical manifestation included fever, fatigue, gastrointestinal symptoms, rash, joint pain and headache. Furthermore, a rare case of acute renal failure associated with acute non-fulminant hepatitis B was observed in our study. The acute renal failure occurred at the 3rd day after acute-onset of acute hepatitis B, and the presence of oliguria lasted for 19 days, anuria for six days. The patient was finally cured by maintenance hemodialysis as well as symptomatic and supportive treatment. Other complications including cholecystitis, lung infection, upper gastrointestinal bleeding, abdominal infection and even bacteremia were observed among patients in the present study. All these results indicated that prevention and treatment of acute hepatitis B should not be ignored and several severe complications would explode among patients with acute hepatitis B.

A majority of patients in our study were diagnosed with acute hepatitis B in time and received proper treatment. Four cases were misdiagnosed with chronic hepatitis B due to the similar clinical manifestation between acute-onset of chronic hepatitis B and acute hepatitis B, especially for cases without positive HBsAg, hepatic dysfunction or chronic hepatic symptoms [18]. Changes of serologic markers and HBV DNA during the disease course can definitely identify the types of hepatitis. Serologic markers including HBsAg, antibodies to hepatitis B core antigen become undetectable and HBV DNA levels begin to decrease, and even become undetectable in 6-12 months after acute infection, while these molecules still exist in persons with chronic infection [1]. One case had ever been diagnosed with diabetic ketoacidosis due to hyperglycemia and detection of ketone body in urine. The symptoms of this patient might be caused by thesignificantly increased level of several hormones including glucagon, cortisol and growth hormone leading to glycometabolic disorder after acute HBV infection [19]. Another case had been considered polymyositis due to hepresented fever, joint and muscle pain. Furthermore, two cases had not been confirmed first, since they had both fever and multi-organ impairment.

In our study, it was found that the hepatic function was greatly improved after receiving hepatoprotective, anti-inflammatory, symptomatic and supportive treatments during hospitalization, and a majority of patients were with good prognosis of an obvious increase of HBsAg seroconversion and HBV-DNA seroconversion after half a year period follow up. There is a controversial opinion of the antiviral therapy on acute hepatitis B [20]. Some scholar considered that antiviral therapy was not necessary in cases of acute HBV infection, but patients should receive nucleotide analogues in a timely manner to inhibit HBV replication and control the disease when the hepatitis begins to develop into severe hepatitis or has the tendency towards severe hepatitis [20]. There were nine patients with fulminant hepatitis. Patients with oral antiviral treatment had been recovered, while among the remaining five cases three of them died during the follow-up. In addition, 9 cases with acute infection of HBV developed into chronic hepatitis B. The consistent presence of hepatitis B virus in vivo and immune dysfunction in human body were the main causes of chronic hepatitis, thus anti-virus and immunoregulation therapies during the early stages remain the therapeutic methods to prevent chronization of hepatitis B. In a previous study of 38 patients with acute hepatitis B treated with anti-viral therapies (lamivudine with ITF α-1b, and the treatment course was three months), the HBsAg became negative in all patients post-treatment, the HBsAb became positive in 92.1% patients, and there was no chronization of hepatitis within the half year follow-up [21]. We suppose that proper treatment according to the development of the disease is essential for the patients with acute hepatitis B.

There are several limitations in our study, of which we are aware. Our study was limited by the small number of patients, short follow-up time, and single center study. Thus, a study of large population, multiple center and long follow-up time should be conducted to further investigate the trends of acute hepatitis B. Besides, we did not apply kidney puncture, so further research about kidney tissue could be practiced to study the mechanism of acute renal failure caused by acute hepatitis.

Conclusion

In conclusion, acute hepatitis B seemed occurred more frequently among adult males

with unknown transmission routes among Chinese population. Several complications associated with acute hepatitis B and the risk for acute hepatitis B developing into chronic infection of HBV should be noticed. In addition, the comprehensive treatment combined with anti-HBV drug is recommended in clinical practice.

Acknowledgements

This study was supported by Science and Technology Research Projects of the Education Department of Heilongjiang province (11551301).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xiaohong Chen, Department of Infectious Diseases, The First Affiliated Hospital of Harbin Medical University, 23 Youzheng Street, Nangang District, Harbin 150001, P. R. China. Tel: +86-451-84883002; Fax: +86-451-84883002; E-mail: chenlred@163.com

References

[1] Shepard CW, Simard EP, Finelli L, Fiore AE and Bell BP. Hepatitis B Virus Infection: Epidemiology and Vaccination. Epidemiol Rev 2006; 28: 112-125.
[2] Rehermann B and Nascimbeni M. Immunology of hepatitis B virus and hepatitis C virus infection. Nat Rev Immunol 2005; 5: 215-229.
[3] Lok AS and McMahon BJ. Chronic hepatitis B: update 2009. Hepatology 2009; 50: 661-662.
[4] Lindh M, Horal P and Norkrans G. Acute hepatitis B in Western Sweden–genotypes and transmission routes. Infection 2000; 28: 161-163.
[5] Seeff LB, Beebe GW, Hoofnagle JH, Norman JE, Buskell-Bales Z, Waggoner JG, Kaplowitz N, Koff RS, Petrini JL Jr and Schiff ER. A serologic follow-up of the 1942 epidemic of post-vaccination hepatitis in the United States Army. N Engl J Med 1987; 316: 965-970.
[6] Lavanchy D. Worldwide epidemiology of HBV infection, disease burden, and vaccine prevention. J Clin Virol 2005; 34: S1-S3.
[7] Wasley A, Kruszon-Moran D, Kuhnert W, Simard EP, Finelli L, McQuillan G and Bell B. The prevalence of hepatitis B virus infection in the United States in the era of vaccination. J Infect Dis 2010; 202: 192-201.
[8] Chang MH. Hepatitis B virus infection. Semin Fetal Neonatal Med 2007; 160-167.
[9] Lok AS and McMahon BJ. Chronic hepatitis B. Hepatology 2007; 45: 507-539.
[10] Alter MJ, Hadler SC, Margolis HS, Alexander WJ, Hu PY, Judson FN, Mares A, Miller JK and Moyer LA. The changing epidemiology of hepatitis B in the United States: need for alternative vaccination strategies. JAMA 1990; 263: 1218-1222.
[11] Kim W, Benson JT, Therneau TM, Torgerson HA, Yawn BP and Melton LJ. Changing epidemiology of hepatitis B in a US community. Hepatology 2004; 39: 811-816.
[12] Kishi T, Ikeda Y, Takashima T, Rikitake S, Miyazono M, Aoki S, Sakemi T, Mizuta T and Fujimoto K. Acute renal failure associated with acute non-fulminant hepatitis B. World J Hepatol 2013; 5: 82-85.
[13] Ring-Larsen H and Palazzo U. Renal failure in fulminant hepatic failure and terminal cirrhosis: a comparison between incidence, types, and prognosis. Gut 1981; 22: 585-591.
[14] Bamber M, Thomas HC, Bannister B and Sherlock S. Acute type A, B, and non-A, non-B hepatitis in a hospital population in London: clinical and epidemiological features. Gut 1983; 24: 561-564.
[15] Kang HM, Jeong SH, Kim JW, Lee D, Choi CK, Park YS, Hwang JH, Kim N and Lee DH. Recent etiology and clinical features of acute viral hepatitis in a single center of Korea. Korean J Hepatol 2007; 13: 495-502.
[16] Kuo A and Gish R. Chronic hepatitis B infection. Clin Liver Dis 2012; 16: 347-369.
[17] Alter MJ. Epidemiology and prevention of hepatitis B. Semin Liver Dis 2003; 23: 39-46.
[18] Custer B, Sullivan SD, Hazlet TK, Iloeje U, Veenstra DL and Kowdley KV. Global epidemiology of hepatitis B virus. J Clin Gastroenterol 2004; 38: S158-S168.
[19] Tian T. Preliminary study of gluco nafe metabolism in acute icterohepatitis patients. Chinese Journal of disease control prevention 1999; 3.
[20] Kumar M, Satapathy S, Monga R, Das K, Hissar S, Pande C, Sharma B and Sarin S. A randomized controlled trial of lamivudine to treat acute hepatitis B. Hepatology 2007; 45: 97-101.
[21] Ma L, Huang Y, Zhang Y, Che X and Wang J. Observation of the progress and effects of anti-virus therapy in acute hepatitis B patients. China Journal of Modern medicine 2005; 15: 3820-3822.