Mod Care J. 2017 January; 14(1):e64726. doi: 10.5812/modernc.64726.

Published online 2016 December 28. **Research Article**

Follow-Up of Chronic Hepatitis B Carriers: A Cross-Sectional Descriptive-Analytical Study

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Received 2016 February 16; **Accepted** 2016 March 26.

Abstract

Background: Hepatitis B is a serious liver infection and one of the 5 leading causes of death around the world. Chronic hepatitis B has a variant natural history. Around one-third of patients with chronic hepatitis may eventually develop cirrhosis or hepatocellular carcinoma. The aim of this study was to follow-up chronic hepatitis B carriers.

Methods: This cross-sectional descriptive-analytical study was done on 235 chronic hepatitis B carriers, who referred to an infectious disease and tropical medicine clinic, in Birjand, Iran. All chronic hepatitis B carriers, who had referred to the study settings from 2005 to 2013, were approached. Data were entered in the SPSS software (v. 21.0) and analyzed via the Chi-square and the Fisher's exact tests at a significance level of less than 0.5.

Results: The majority of participants were male (132 cases, 56.2%) and married (193 cases, 82.1%) and were aged 33.3 $\pm$ 0.7. The follow-up mean time was 5 years with a range of 3 to 9 years. During this follow-up period, 10 individuals (4%) experienced seroconversion from hepatitis B surface antigen (HBsAg) positivity to negativity, 35 (15%) developed active hepatitis, 8 (3.5%) developed cirrhosis, and 2 (1%) developed liver cancer. The remaining 180 participants (76.5%) had inactive hepatitis. Among participants, 45 (19%) were hepatitis B e antigen-positive, 24.5% of whom experienced positivity to negativity seroconversion.

Conclusions: Most chronic hepatitis B carriers are primarily asymptomatic. However, 15% developed serious liver disease over time. Therefore, careful lifelong follow-up assessments are needed for early diagnosis and prevention.

Keywords: Natural History, Chronic Hepatitis B, Hepatitis B Carriers

1. Background

Viral hepatitis virus (HBV) infection is among 5 infectious causes of early death around the world (1). More than 400 million people around the world have HBV infection (2). It is the leading cause of more than 50% of acute hepatitis, 85% of cirrhosis, and about 70% of chronic hepatitis in Iran (3). Based on the reports of the world health organization and the center for disease control and prevention, Iran is located in the intermediate endemicity region of hepatitis B (4). The prevalence of HBV infection in Iran is 2.2% (5). In Birjand, Iran, the prevalence is 1.6% (6). Estimates show that about 1.5 million Iranians have HBV infection (7).

The risk factors of HBV infection in Iran are positive family history of HBV infection, blood transfusion, hospitalization, unprotected sexual contact, masculinity, and urban residence (8).

Despite its acute and benign nature, HBV infection in younger age groups could increase the risk of cirrhosis and hepatocellular carcinoma at older ages (9). This infection can cause serious liver diseases, such as cirrhosis and liver cancer. A study reported that 15% to 40% of Iranians with HBV infection are at risk for cirrhosis or hepatocellular carcinoma (7). If remained untreated, patients with chronic hepatitis B (CHB), who enter the acute phase of hepatitis, may develop complications, such as cirrhosis, hepatocellular carcinoma, liver failure, and eventually death (4, 8, 9).

Given the serious complications and the high mortality rate of HBV infection, early diagnosis of HBV infection and assessment of its severity and natural history are of great importance. However, there is no credible information about HBV infection in Birjand, Iran. Therefore, the present study was done to assess the natural history and the outcomes of HBV infection among CHB carriers.

2. Methods

This cross-sectional descriptive-analytical study was done on 235 CHB carriers, who referred to an infectious disease and tropical medicine clinic in Birjand, Iran. Carriers

were included if they had been monitored for HBV infection for at least 3 consecutive years during 2005 to 2013. The exclusion criterion was a positive hepatitis C virus antibody test. Sampling was done through the census method and a researcher-made checklist was used for data collection. Checklist items were age, gender, employment and marital status, the route of obtaining informed about their affliction by HBV infection, and the results of para-clinical tests. The checklist was completed based on patients' medical records and the SPSS software (v. 21.0) was employed to analyze the data. The correlation of HBV infection outcome with other variables was assessed via the Chi-square and the Fisher's exact tests at a significance level of less than 0.5. The data were presented using absolute and relative frequencies.

The ethical considerations were approved by the ethical committee of Birjand University of medical sciences under code ir.bums.REC.1394.189.

3. Results

This study was done on 235 CHB carriers. Participants were mostly male (132 cases, 56.2%) and married (193 cases; 82.1%). Participants had been diagnosed with HBV infection, based on the results of routine periodical laboratory tests (70 cases; 30%), the results of laboratory tests performed in the process of blood donation (56 cases; 24%), after the detection of the infection among other family members (54 cases; 22.5%), during pregnancy-related assessments (51 cases; 22%), or at the time of HBV vaccination (4 cases; 1.5%).

Overall, 60.4% of participants had no risk factor for HBV infection. Risk factors for HBV among the remaining participants were surgery (13.6%), endoscopy (10.6%), fighting in war (6.4%), cupping therapy (4.3%), tattoo (1.7%), alcohol consumption (1.3%), blood transfusion (1.3%), and foreign travel (0.4%).

The follow-up assessment mean time was 5 years with a range of 3 to 9 years. At the end of the follow-up assessment, 10 participants (4%) experienced seroconversion from hepatitis B surface antigen (HBsAg) positivity to negativity. On the other hand, 180 cases (76.5%) remained as CHB carriers, 35 cases (15%) developed active CHB, 8 cases (3.5%) developed cirrhosis, and 2 cases (1%) developed liver cancer. During the time interval of the study, 3 CHB carriers died, 2 (67%) experienced cirrhosis and 1 (33%) developed cirrhosis and hepatocellular cancer (Table 1). The results of the Fisher exact test showed that HBeAg positivity was significantly correlated with disease outcome (P = 0.026).

Among participants, 45 (19%) were HBeAg-positive. At the end of the follow-up assessment period, 23 (51%) had inactive hepatitis, 11 (24%) had active hepatitis, 1 (2.5%) had cancer, and 10 (22.5%) showed seroconversion from HBeAg positivity to negativity. The results of the Fisher's exact test showed that HBeAg was significantly correlated with disease outcome, in that active CHB and carcinoma among HBeAg-positive individuals were more common than their HBeAg-negative counterparts (P = 0.026; Table 2). However, HBeAg was not significantly correlated with hepatitis-related death (P = 0.06). The results of the Chi-square test illustrated that hepatitis outcomes among male carriers were significantly more common than female carriers (P = 0.022). Finally, the findings revealed that the prevalence of hepatitis D virus (HDV) infection among participants was 1.7%.

Table 1. Demographic and Clinical Characteristics of Chronic Hepatitis B Carriers

Characteristics	Frequency	Percent
Gender		
Male	132	56.2
Female	103	43.8
Age group		
Less than 30	105	44.6
30 and more	130	55.4
Marital status		
Single	35	14.9
Married	193	82.1
Divorced	1	0.4
Widowed	6	2.6
HDV antibody		
Positive	4	1.7
Negative	231	98.3
Fatty liver disease		
Yes	33	15.1
No	185	84.9
HBeAg at admission		
Negative	190	80.9
Positive	45	19.1
HBsAg after follow-up		
Negative	10	4
Positive	225	95.7
HBeAg follow-up		
Negative	201	85.5
Positive	34	14.5

4. Discussion

This study was done on 235 CHB carriers in South Khorasan, Iran. Carriers had been monitored for at least 3 consecutive years. During the study, 10 carriers (4%) became HBsAg-negative. In line with this finding, previous studies reported a positive-to-negative seroconversion rate of 2.7% (10), 6% (11), and 3.1% (12).

Table 2. The Outcomes of Chronic Hepatitis B Infection[a]

Inactive Carrier at Admission	The Outcomes After the Follow-Up Period				
	Inactive	Active	Cirrhosis	Cancer	HBsAg Seroconversion
Total, N = 235	180 (76.5)	35 (15)	8 (3.5)	2 (0.8)	10 (4)
HBeAg Positive, N = 45	23 (51)	11 (24.5)	0 (0)	1 (2.5)	10 (22.5)
HBeAg Negative, N = 190	157 (82.5)	24 (12.5)	8 (4.5)	1 (0.5)	0 (0)

[a] Values are expressed as No. (%).

At the beginning of the study, 45 participants (19%) were HBeAg-positive and 190 (81%) were HBeAg negative. Previous studies reported an HBeAg positivity rate of 2.5% to 29.4% (10, 13-15). Moreover, HBeAg seroconversion rate in the present study was 24.5%, while this rate in previous studies was 10.5% (10), 13.3% (16), 30% (17), and 10% (18). Seroconversion is affected by factors, such as precore mutation, the phase of hepatitis, and the age when afflicted by HBV infection.

Among 235 CHB carriers in this study, 15% (35 in total) entered the active phase of hepatitis. The rates of entering the active phase of the disease among HBeAg-positive and HBeAg-negative carriers were 24.5% (eleven out of 45 cases) and 12.5% (24 out of 190 cases), respectively. An earlier study in Iran also showed that among 22 HBeAg-positive individuals, 18 developed active CHB (10). The findings also showed that CHB and carcinoma among HBeAg-positive carriers were more prevalent than their HbeAg-negative counterparts. Similarly, an earlier study indicated that compared with HBeAg-negative and female individuals, liver disease was significantly more severe among HBeAg-positive and male individuals, respectively (19). Another study also reported a significant correlation between HBeAg positivity and HBV infection complications, such as cirrhosis and hepatocellular carcinoma (20). All these findings confirm that HBeAg positivity is correlated with hepatitis progression and severity.

Furthermore, HDV infection rate in the current study was 1.7%. Previous studies from Iran reported that HDV infection rate was 3.1% (21), 2% (22), and 6.61% (23). The difference among different studies regarding HDV infection rate could be attributed to differences in hepatitis risk factors and transmission routes, as HDV infection is apparently more prevalent among injection drug users and those with frequent blood transfusion. Other factors behind such differences may be differences in socioeconomic status and health-related behaviors of people in different areas of Iran.

The participants of the current study had been informed about their affliction by HBV infection during routine periodical laboratory tests (30%) and blood donation process (24%), by detection of the infection among other family members (22.5%), through pregnancy-related assessments (22%), or request for HBV vaccination. The principal routes for obtaining information about HBV affliction in a study in India were blood donation (36.8%) and pregnancy-related assessments (29.2%) (14). Another study also showed blood donation (63.5%) and pregnancy-related assessments (26.5%) as the most common routes (24). These findings confirm that most infected people are unaware of their affliction by HBV infection and highlight the importance of HBV assessment before or during pregnancy in order to adopt effective measures to prevent mother-to-child infection transmission.

4.1. Conclusion

The results of this study show that most patients with CHB have no evident clinical or laboratory manifestations, while 15% of them develop severe liver disease over time. Therefore, careful lifelong follow-up assessments are needed for early diagnosis and prevention.

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