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ORIGINAL ARTICLE

Long-term Follow-up Study of Asymptomatic HBsAg-Positive Carrier

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ABSTRACT

Objectives: Hepatitis B virus (HBV)-related chronic liver disease is a common health problem in our country. About 5.2 to 7.8% population of Bangladesh is chronic HBV carriers. There is no long-term follow-up study of asymptomatic HBV carriers in our country. Aim of the present study is to know the outcome of these cases in 10 years.

Materials and methods: Twelve hundred and eighty-six cases of asymptomatic HBsAg-positive individuals were evaluated and followed up for 10 years at gastroenterology department, combined Military Hospital, Dhaka Cantonment, from January 2000 to December 2009.

Results: Age of the patient's ranges from 3 to 50 years (mean, 27 ± 6 years). Majority cases were males 1,236 (96.12%). Baseline alanine aminotransferase (ALT) ≥45 IU/l was found in 168 (13.06%) cases. Ultrasonography revealed coarse hepatic echotexture in 62 (5.63%) cases out of 1,200 cases. Hepatic histology revealed chronic hepatitis in 318 cases (35.02%) and cirrhosis of liver in 24 cases (2.64%), hepatocellular carcinoma 1 (0.11%), fatty liver in eight (0.88%) out of 908 cases. After follow-up, compensated cirrhosis of liver was found in 90 (15%) cases, decompensated liver disease in 50 (8.33%) cases and hepatocellular carcinoma (HCC) in 42 (7%) out of 600 cases. Twenty (3.33%) cases died due to liver failure, HCC and other complications. Spontaneous HBsAg seronegativity occurred in five cases out of 600 cases (0.83%), and spontaneous HBeAg seroconversion occurred in 10 cases out of 180 cases (5.55%).

Conclusion: Asymptomatic HBsAg-positive carriers should not be considered as inactive disease. They should be followed up every 3 to 6 months to know activity of the disease and development of complications. Antiviral treatment should be instituted in cases of active liver disease.

Keywords: HBV carrier, Long-term follow-up, Asymptomatic versus disease free.

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INTRODUCTION

Chronic hepatitis B viral infection is a chronic health problem leading to serious morbidity and mortality in Bangladesh. Prevalence of hepatitis B virus (HBV) in Bangladesh ranges from 5.2 to 7.8%. It is the leading cause of chronic liver diseases in Bangladesh.[1-3] Chronic hepatitis B viral infection leads to chronic hepatitis, cirrhosis of liver, hepatocellular carcinoma and liver failure. Worldwide, about 350 to 400 million chronic carriers are present.[4] Aim of this study is to know the long-term outcome of asymptomatic chronic carriers of hepatitis B virus in Bangladesh.

MATERIALS AND METHODS

This study was carried out at Gastroenterology Department, Combined Military Hospital, Dhaka Cantonment, from January 2000 to December 2009. Asymptomatic HBsAg-positive cases were enrolled in the register consecutively. HBsAg was detected during screening test for going abroad, UN mission, blood donation and vaccination. A total of cases 1,286 were registered for study. All the cases were evaluated by thorough clinical examination. HBsAg, HBeAg, Anti-HBe, alanine aminotransferase (ALT), prothrombin time (PT), serum albumin, alfafetoprotein (AFP) and ultrasonography (USG) of liver were done in all cases. Liver biopsy was done in 908 cases and HBV DNA was tested in selected cases.

Those who had positive HBeAg, raised ALT (≥2 times the upper limit of normal) and HBV DNA $\geq 10^5$ copies/ml were given antiviral treatment and were excluded from study. All cases were followed up 6 monthly. At all visits they were assessed clinically, biochemically and ultrasonographically to see progression of the disease.

RESULTS

The main characteristic features of the subjects at base line are given in Tables 1 to 5. The mean age of the patient was 27 ± 6 years (range, 3-50 years). Majority of cases were male (1236; 96.13%). In 1,195 cases (92.92%), no risk factors for HBV infection was found. In 20 cases (1.55%), health care workers and in 30 cases (2.33%) other family members of the patient were infected (Table 1). Most of the patients were asymptomatic (1,195; 92.92%) but some complained of right hypochondrial pain (50; 3.88%) and fatigue (25; 1.94%) (Table 2). HBV DNA was positive in 15 out of 20 cases (75%), ALT ≥ 45 IU/l was found in 168 cases (13.06%) (Table 3). Ultrasonography revealed coarse hepatic echotexture in 62 cases (5.16%) (Table 4). Liver biopsy was done in 908 cases of which chronic hepatitis was found in 318 cases (35.02%), cirrhosis of liver in 24 cases (2.64%), fatty liver in eight cases (0.88%) and

Table 1: Baseline characteristics and risk factor HBV carriers (n = 1,286)

Characteristics	*no*	*%*
• Age (year): 3-50 (mean 27 ± 6)		
• Sex:		
– Male	1,236	96.12
– Female	50	3.88
• Previous blood transfusion	5	0.38
• Previous jaundice	18	1.39
• Contact with jaundice case	03	0.23
• Affected health care workers	20	1.55
• Affected family members	30	2.33
• Previous hospital admission	15	1.16
• Unknown risk factors	1,195	92.92

Table 2: Baseline clinical features of HBV carriers (n = 1,286)

Characteristics	*no*	*%*
• Asymptomatic	1,195	92.92
• Pain in right hypochondrium	50	3.88
• Fatigue	25	1.94
• Anorexia	5	0.38
• Hepatomegaly	4	0.31
• Splenomegaly	5	0.38
• Spider angioma	2	0.15

Table 3: Baseline serological and biochemical features of HBV carriers (n = 1,286)

Characteristics	*no*	*%*
• HBsAg +ve	1,286	100
• ALT ≤ 45(IU/l)	1,118	86.93
• ALT 45(IU/l)	168	13.06

Table 4: Baseline USG features of HBV carriers (n = 1,200)

Characteristics	*no*	*%*
• Coarse echotexture	62	5.63
• Normal echotexture	1,138	94.37

Table 5: Baseline histological features of HBV carriers (n = 908)

Characteristics	*no*	*%*
• Chronic hepatitis (mild)	294	32.37
• Chronic hepatitis (moderate)	19	2.09
• Chronic hepatitis (mild)	05	0.55
• Cirrhosis	24	2.64
• HCC	01	0.11
• Fatty change	08	0.88
• Normal	557	61.34

Table 6: Clinical outcome after 10 years follow-up of HBV carriers (n = 600)

Characteristics	*no*	*%*
• Cirrhosis	90	15.0
• Liver failure	50	8.33
• HCC	42	7.0
• Death	20	3.33
• Spontaneous HBsAg negativity	5	0.83
• Spontaneous HBeAg seroconversion (n = 180)	10	5.55

hepatocellular carcinoma in 1 case (0.11%) (Table 5). Six hundred cases were followed up for prolonged duration. Cirrhosis of liver was found in 90 cases (15%), liver failure in 50 cases (8.33%), hepatocellular carcinoma in 42 cases (7%). Twenty patients (3.33%) died during this period due to liver failure, hepatocellular carcinoma and other complications (Table 6). Spontaneous HBsAg seronegativity was found in five cases (0.83%), spontaneous HBeAg seroconversion was found in 10 out of 180 cases (5.55%).

DISCUSSION

Hepatitis B virus is the leading cause of chronic liver disease, cirrhosis of liver, hepatocellular carcinoma and liver failure in China, South East Asia, including Bangladesh and Africa.[5] Asymptomatic carriers are very prevalent in these regions. Majority of these asymptomatic carriers are diagnosed during screening test for vaccination, blood donation, going abroad or during routine tests for some other reasons. They usually do not suffer from acute viral hepatitis. The reason for this is that they probably contract the disease in perinatal period or early childhood. In early childhood or perinatal infection, acute hepatitis is rare. More than 90% of these cases lead to chronicity.[6] During the natural course of the disease, some may develop chronic hepatitis, cirrhosis of liver, hepatocellular carcinoma and liver failure. Spontaneous HBeAg seroconversion (HBeAg negative and anti HBe positive) occurs in majority of the cases but HBsAg seronegativity is rare. Annual incidence of spontaneous HBsAg seroclearance is 0.1 to 0.8% in high endemic areas and 1.0 to 2.1% in low endemic areas.[7] Presence of HBsAg in serum means presence of ccc DNA (covalently closed circular DNA) in the hepatocyte nuclei. So long ccc DNA is present in the nuclei of hepatocyte, there will be possibilities of complications and death due to liver disease. HBsAg seroclearance is associated with reduced complications and hepatocellular carcinoma and it is considered as closest to cure.[8] In our study, 1,286 cases of asymptomatic HBsAg-positive individuals were initially evaluated and followed up. After 10 years, cirrhosis of liver occurred in 15%, liver failure in 8.33% and hepatocellular carcinoma in 7% of cases out of 600 cases. HBeAg seroconversion occurred in 5.55% and HBsAg seroclearance in 0.83% cases. Spontaneous HBeAg seroconversion was found in 91.83% at the time of entry into the study. Mortality rate during this period was 3.33%. Fatovich et al showed liver-related death in 15.7%, cirrhosis of liver in 24.3%, spontaneous HBeAg seroconversion in 87% of case after 25 years of follow-up in Caucasion patients.[9] Higher rate of death and development of cirrhosis in this study may be due to longer duration of follow-up and different race

involved in study population. In our study, higher rate of spontaneous HBeAg seroconversion to anti-HBe at study entry may be due to higher age of study population. One patient developed reactivation of HBV replication following cancer chemotherapy for breast cancer.[10]

CONCLUSION

Asymptomatic HBsAg-positive carriers should not be considered as inactive disease. They may progress to cirrhosis of liver, hepatocellular carcinoma, liver failure and death during the natural course of disease. So, they should be followed up every 3 to 6 months to know activity of the disease and development of complications. Antiviral treatment should be instituted in all cases of active liver disease.

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