

## ORIGINAL ARTICLE

# FREQUENCY OF CHRONIC ACTIVE HEPATITIS IN ASYMPTOMATIC HBV CARRIERS IN BABOL, IRAN

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### Abstract

**Background-** Hepatitis B virus (HBV) infection is a major worldwide health problem. Most of the patients are asymptomatic and at risk of developing chronic liver disease, cirrhosis and hepatocellular carcinoma. The aim of the present study was to determine the frequency of chronic active hepatitis in asymptomatic HBV carriers in Babol, northern Iran.

**Methods-** This study was performed in 410 HBV carriers older than 15 years who were diagnosed by positive serum hepatitis B surface antigen (HBsAg) from January 1998 to September 2000. Family members of infected patients were also screened. For each patient, HBsAg, hepatitis B early antigen (HBeAg), hepatitis B early antibody (HBeAb) and alanine aminotransferase (ALT) were measured at the time of screening and again 6 months later. In patients with raised ALT, liver biopsy was performed and a Knodell score  $\geq 4$  was considered as chronic active hepatitis. Proportions were then analyzed using the chi-square test.

**Results-** Of the 410 patients, 229 (53.3%) were males and 181 (46.5%) were females. Mean age  $\pm$  standard deviation (SD) was  $28 \pm 12.7$  years. Of these, 362 (88.3%) were HBeAb-positive and 48 (11.7%) were HBeAg-positive. ALT was elevated in 73 (17.8%) of patients. Chronic active hepatitis was found in 8% and 10.4% of the HBeAb-positive and HBeAg-positive cases, respectively ( $p = 0.57$ ). Chronic hepatitis was significantly higher in males than females ( $p = 0.0001$ )

**Conclusion-** The results show that the frequency of chronic active hepatitis is high in asymptomatic HBV carriers. It is almost equal in HBeAb-positive and HBeAg-positive cases and is higher in males than females. Assessment of HBV precore mutants in anti-HBeAg-positive cases is highly recommended.

**Keywords** • alanine aminotransferase • carrier state • hepatitis B early antigen • hepatitis B surface antigen • hepatitis B virus infection

### Introduction

More than 5% of the world's population have chronic hepatitis B virus (HBV) infection, which is the leading cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma.<sup>1-3</sup> About 20% of individuals with this infection have chronic active hepatitis (CAH).<sup>4</sup>

More than 3% of the general population in Iran have chronic HBV infection and are asymptomatic.<sup>3</sup> Near 8000 to 10,000 deaths occur

each year due to its sequelae in Iran.<sup>3</sup> Early diagnosis and treatment of CAH may arrest or delay the progression of HBV-associated hepatic injury and lead to histologic improvement and suppression of viral replication.<sup>1,5,6</sup> Because most HBV carriers are asymptomatic, this study was performed to evaluate the frequency of CAH in asymptomatic HBV carriers among blood donors in Iran.

### Materials and Methods

From January 1998 to September 2000, all HBsAg-positive individuals older than 15 years

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## Frequency of Chronic Active Hepatitis in Asymptomatic HBV Carriers

**Table 1.** Characteristics of 410 HBV carrier patients.

Characteristic	Male No.	Female No.	Total (%)
HBeAb positive	201	161	362 (88.3)
- Elevated ALT (>40 IU/L)	36	27	63 (15.3)
HBeAg positive	28	20	48 (11.7)
- Elevated ALT (>40 IU/L)	7	3	10 (2.4)

ALT = alanine aminotransferase

who had been screened at Babol Blood Bank were studied. The family members of infected individuals were also included in the study. All patients with positive HBsAg were tested for hepatitis B early antigen (HBeAg), hepatitis B early antibody (HBeAb) and alanine aminotransferase (ALT), and the measurements were repeated 6 months later. An ALT greater than 40 IU/L was considered abnormal and after obtaining written consent, a liver biopsy was obtained from those patients who had an elevated ALT level. Liver biopsy samples were scored for necroinflammation and fibrosis according to Knodell scoring system, which is the sum of periportal necrosis, intralobular necrosis, portal inflammation and fibrosis.<sup>7</sup> Patients with Knodell score of  $\geq 4$  were considered to have CAH. Proportions were analyzed using the chi-square test, and the results were considered statistically significant when the  $p$  value was less than 0.05.

### Results

A total of 410 HBsAg-positive patients were studied. Of them, 229 (55.9%) were males and 181 (44.1%) were females, with a mean age ( $\pm$  standard deviation, SD) of  $28 \pm 12.7$  years. HBeAb was positive in 362 (88.3%) patients. Forty-eight (11.7%) patients were HBeAg-positive. The characteristics of the study population are shown in Table 1.

ALT level was elevated in 63 of 362 (17.4%) patients positive for HBeAb and 10 of 48 (20.8%) patients positive for HBeAg. A liver biopsy was performed in all patients with elevated ALT. Thirty-four patients (8.3%) had a Knodell score ranging from 4 to 13 (median, 7).

Twenty-nine of 362 (8%) HBeAb-positive patients and five of 48 (10.4%) HBeAg-positive patients had CAH. The frequency of CAH was 8.3% (34/410) among all patients with HBV infection studied. No significant difference was seen in the frequency of CAH between HBeAb-positive and HBeAg-positive patients ( $p = 0.57$ ). The frequency of CAH was 14% (32/229) in males

and 1% (2/181) in females ( $p = 0.0001$ ). A history of icteric hepatitis B was found in 15 (3.6%) patients.

### Discussion

In our study, the frequency of HBeAb-positive chronic HBV infection (88.3%) was similar to that of other studies in Iran and the Mediterranean area<sup>3,8</sup> but differed from the results reported from France and the USA (22% and 54% respectively).<sup>9,10</sup> Eight percent of HBeAb-positive patients in our study had active hepatitis. In a study from Hong Kong, 37% of HBeAb-positive patients had active hepatitis.<sup>11</sup> In another study, in Auckland, New Zealand, 96% of the patients with HBeAb had active hepatitis.<sup>12</sup> A study from China revealed that 70% of HBeAb-positive patients had active hepatitis.<sup>13</sup> Studies in western countries also show a high prevalence of active hepatitis in HBeAb-positive patients.<sup>9,14</sup> The high frequency of active hepatitis in the study of other countries may be due to the high percentage of precore mutants and alcohol consumption.<sup>8,13</sup> HBeAb-positive chronic hepatitis B is highly endemic in the Mediterranean area and more than 95% of the patients are infected with HBV mutants.<sup>8</sup>

Alcohol consumption may accelerate the course of liver injury and its progression to cirrhosis, which is caused by persistent HBV infection. Therefore, alcohol consumption is considered to be the most important cause of liver cirrhosis in western countries.<sup>13</sup>

Patients with active hepatitis develop fibrosis of the liver, and later, cirrhosis.<sup>7,13</sup> The frequency of HBeAg-positivity in our study was 12%, which is comparable to the data reported from Sub-Saharan Africa (20.5%)<sup>15</sup> but lower than the 40% prevalence reported in the Far East.<sup>16</sup> Another study in the USA showed that the prevalence of HBeAg-positive patients with chronic HBV infection was 34.4%.<sup>10</sup> The presence of HBeAg in the serum indicates active viral replication, higher infectivity and a potential for more extensive liver damage.<sup>7,10</sup> In our study, 10.4% of HBeAg carriers

had active disease. An American study showed a higher prevalence of active hepatitis in HBeAg carriers.<sup>10</sup> In our study, the prevalence of active hepatitis in HBeAg-positive and HBeAb-positive chronic HBV-infected patients was similar, and active hepatitis was more common in males than females. Similar results were also reported by Toukan in Jordan.<sup>17</sup>

In our study, 96.6% of the patients had no prior history of icteric hepatitis. It may be concluded that infection had occurred perinatally, or early in childhood, because it is usually asymptomatic (which is the case in Iran).

More than 2 million individuals in Iran are asymptomatic HBV carriers<sup>3</sup> and about 8% of them have CAH. It is, therefore, necessary to increase the public awareness, as well as that of the health authorities, about chronic HBV infection. In this way, more asymptomatic HBV carriers with active hepatitis will be identified and counseled.

### Acknowledgments

The authors thank Dr. M. Haji-Ahmadi for performing statistical analysis and Dr. J. Soleimani for laboratory testing.

### References

- 1 Mahoney FJ. Update on diagnosis, management, and prevention of hepatitis B virus infection. *Clin Microbiol Rev.* 1999; **12**: 351-66.
- 2 Dienstag JL, Schiff ER, Wright TL, et al. Lamivudine as initial treatment for chronic hepatitis B in the United States. *N Engl J Med.* 1999; **341**: 1256-62.
- 3 Maraat S, Malekzadeh R, Rezvan H, et al. Hepatitis B in Iran. *Arch Iranian Med.* 2000; **3**: 192-201.
- 4 Ter Borg F, Ten Kate FJ, Cuyppers HT, et al. Relation between laboratory test results and histological hepatitis activity in individuals positive for hepatitis B surface antigen and antibodies to hepatitis B e antigen. *Lancet.* 1998; **351**: 1914-8.
- 5 Mazzella G, Saracco G, Festi D, et al. Long-term results with interferon therapy in chronic type B hepatitis: a prospective randomized trial. *Am J Gastroenterol.* 1999; **94**: 2246-50.
- 6 Imperial JC. National history of chronic hepatitis B and C. *J Gastroenterol Hepatol.* 1999; **14**: 1-5.
- 7 Dienstag JL, Isselbacher KJ. Chronic hepatitis. In: Fauci AS, Harrison TR, eds. *Harrison's Principles of Internal Medicine.* 14th ed, New York: McGraw-Hill. 1998.
- 8 Oliveri F, Santantonio T, Bellati G, et al. Long-term response to therapy of chronic anti-HBe-positive hepatitis B is poor independent of type and schedule of interferon. *Am J Gastroenterol.* 1999; **94**: 1366-72.
- 9 Zarski JP, Marcellin P, Cohard M, et al. Comparison of anti-HBe-positive and HBe-antigen-positive chronic hepatitis B in France. French Multicenter Group. *J Hepatol.* 1994; **20**: 636-40.
- 10 Evants AA, Fine M, London WT. Spontaneous seroconversion in hepatitis B e antigen-positive chronic hepatitis B: implications for interferon therapy. *J Infect Dis.* 1997; **176**: 845-50.
- 11 Chan HL, Leung NW, Hussain M, et al. Hepatitis B e antigen negative chronic hepatitis B in Hong Kong. *Hepatology.* 2000; **31**: 763-8.
- 12 Gane E. Chronic hepatitis B virus infection in South Auckland. *N Z Med J.* 1998; **111**: 120-3.
- 13 Yu AW, Hsu FC, Sheen IS, et al. Prospective study of hepatocellular carcinoma and liver cirrhosis in asymptomatic chronic hepatitis B virus carriers. *Am J Epidemiol.* 1997; **145**: 1039-46.
- 14 Viola LA, Barrison IG, Coleman JC, et al. Natural history of liver disease in chronic hepatitis B surface antigen carriers. Survey of 100 patients from Great Britain. *Lancet.* 1981; **2**: 1156-9.
- 15 Kew MC. Progress towards the comprehensive control of hepatitis B in Africa: a view from South Africa. *Gut.* 1996; **38**: 31-6.
- 16 Bisharat N, Elias M, Raz R, Flatau E. Familial pattern of infection with hepatitis B virus among immigrating Ethiopian Jews in Israel. *Eur J Epidemiol.* 1998; **14**: 89-91.
- 17 Toukan AU. Hepatitis B in the Middle East: aspects of epidemiology and liver disease after infection. *Gut.* 1996; **36**: 2-4.