Prevalence of hepatitis B virus infection among alcoholic patients with liver disease

M ORHOLM, J ALDERSHVILE, U TAGE-JENSEN, P SCHLICHTING, JO NIELSEN, F HARDT, P CHRISTOFFERSEN

From the Division of Hepatology and Department of Pathology, Hvidovre Hospital and 2nd Department of Medicine, Kommunehospitalet, Copenhagen, Denmark

SUMMARY The aim of this investigation was to elucidate a possible role of hepatitis B virus (HBV) in the pathogenesis of liver diseases in alcoholics.

Two hundred and fifty-three alcoholics with liver disease were admitted to two medical departments in Copenhagen during a 15 months period. Seventy-nine patients (31%) showed serological signs (HBsAg, anti-HBs) of previous or active HBV infection. This is a significantly higher prevalence than found in an age-matched control population. Among the 79 patients with HBV markers, a total of 11 was found to be HBsAg-positive. From these 11 patients liver specimens were available for re-evaluation in nine cases. In only three of these liver biopsies, morphological changes indicating alcohol as the aetiological cause were found.

In conclusion, different or concomitant aetiology must be considered in alcoholics with liver disease.

Though the mechanism is still under dispute there is no doubt that alcohol consumption is the cause of the majority of chronic liver diseases occurring in Northern Europe. In these diseases the suspicion of an aetiological role of alcohol is often supported by morphological changes in the liver but just as often exclusively on the anamnestic information of alcohol consumption. However, the risk is to misjudge the importance of alcohol, as information given by the patients may not always be reliable,¹ and thus the importance of alcohol in the pathogenesis may be over- or underestimated.²

By means of specific serological tests for detection of hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs) we have re-evaluated 253 patients previously diagnosed as having an alcoholic liver disease. The liver biopsies from the patients with circulating HBsAg were morphologically re-evaluated.

Patients and methods

In the period from 1 January 1976 to 1 April 1977 a total of 519 patients with liver disease were admitted to the Division of Hepatology, Hvidovre Hospital and 2nd Department of Medicine, Kom-

mune-hospitalet, Copenhagen, Denmark. In 445 of these 519 patients (86%) a liver biopsy was performed.

Two hundred and fifty-three of the patients had been diagnosed as having alcoholic liver disease and form the group in our study. Of these 253 patients a histological diagnosis was available in 205 (81%). The sex ratio between men and women was 2:1. The mean age was 51 yr (range 17-82 yr).

The diagnosis was based on anamnestic information of a daily intake of at least 50 g of alcohol for five years and on clinical, biochemical, and histological findings.

Frozen serum samples from the time of admission to hospital were investigated for hepatitis B surface antigen (HBsAg) and anti-body (anti-HBs) using solid phase radioimmunoassays (Ausria-II and Ausab, Abbott, North Chicago, USA). The analysis were performed under code without knowledge of the clinical or histological diagnosis.

Results

HBsAg was found in 11 of the 253 samples (4%) and anti-HBs in 70 samples (28%). Samples from two patients contained both HBsAg and anti-HBs, hence a total of 79 out of 253 patients (31%) demonstrated serological signs of previous or active HBV infection.

The distribution of age and HBV markers in the

Table 1 The distribution according to age and HBV markers among 253 alcoholic patients with liver disease

Age (yr)	Total No of patients	No of patients with circulating HBsAg or anti-HBs, or both	(%)
15-34	32	10	(31)
35-44	54	10	(19)
45-54	57	19	(33)
55-64	74	24	(32)
65-74	32	14	(44)
75-84	4	2	(50)
Total	253	79	(31)

253 patients is shown in Table 1. An increasing frequency of HBV markers was found with increasing age. In patients above 64 yr, 16 of 36 patients (44%) had HBV markers.

The distribution of HBV markers correlated with histological diagnosis is shown in Table 2. No significant difference in the prevalence of anti-HBs was demonstrated between the histological subgroups. In contrast, among the patients with a histological diagnosis HBsAg was only found in the group with macronodular cirrhosis. From nine of the 11 HBsAg-positive patients bioptic specimens originally diagnosed as cirrhosis were available for re-evaluation. Three biopsies showed alcoholic hepatitis with Mallory bodies and Edmonson's fibrosis³ indicating alcohol as the aetiological factor. Ground-glass appearance³ was found in a total of three patients one of whom had alcoholic hepatitis. On the basis of histological findings no signs of alcoholic liver disease were found in 6 patients. All the nine patients had macronodular cirrhosis of the liver—one with a simultaneous liver cell carcinoma—and all had various degrees of bile duct proliferation. Thus persistent HBV infection as an aetiological factor may be implicated in at least 6 patients primarily classified as having alcoholic liver disease.

The prevalence of HBV markers among the 253 alcoholics with liver disease in relation to age is shown in the Figure. For a comparison the corre-

Correlation between prevalence of HBV markers and age classes in 253 alcoholics with liver disease ($p < 0.05$, $r = 0.85$). For comparison, note the prevalence found among Danish surgeons and dentists of whom, however, none was HBsAg-positive.

sponding prevalences found among Danish surgeons⁴ and dentists⁵ are shown. However, it should be noticed that HBsAg was not found in any of the surgeons or dentists. In the present series a significant correlation was found between age and presence of HBV markers ($p < 0.05$) with $r = 0.85$.

Discussion

The prevalence of HBsAg in the Danish population is 0.1-0.2%⁶ and the prevalence among alcoholics with liver disease found in this work (4%) is thus approximately twenty times as high.

As compared to the prevalence among dentists (Figure), the higher prevalence of HBV markers among alcoholics with liver disease is not solely explained by the high prevalence of HBsAg but also by an increased prevalence of anti-HBs. This suggests

Table 2 Distribution of HBV markers and histological diagnosis among 253 patients with chronic alcoholism and liver disease

Serological findings	Micronodular cirrhosis (%)		Macronodular cirrhosis (%)		Alcoholic hepatitis (%)	Steatosis (%)	No biopsy or biopsy not available	Total No of patients
	without alcoholic hepatitis	with alcoholic hepatitis	without alcoholic hepatitis	with alcoholic hepatitis				
HBsAg and anti-HBs negative	26 (67)	39 (71)	11 (48)	2 (40)	7 (78)	60 (81)	29	174
anti-HBs positive	13 (33)	16 (29)	6 (26)	0 (0)	2 (22)	14 (19)	17	68
HBsAg-positive	0 (0)	0 (0)	6 (26)	3 (60)	0 (0)	0 (0)	2	11

a higher exposure to HBV among alcoholics with liver disease. However, Danish surgeons do not differ in prevalence of HBV markers, but in contrast to alcoholics with liver disease no surgeons were found to be HBsAg-positive. The finding of HBsAg in 4% of the patients in the present study may reflect inclusion of chronic type B hepatitis in the group of patients with alcoholic liver disease. However, it cannot be ruled out that the increased prevalence of HBsAg carriers may be due to a compromised immune responses in the alcoholics as seen in patients with Down's syndrome,⁷ patients in haemodialysis,^{8,9} etc.

Re-evaluation of the liver histology of the HBsAg-positive alcoholics with the aim of distinguishing between alcoholic and/or viral aetiology of the liver disease only suggested alcoholic aetiology in three of the nine biopsies. Thus the aetiology of the liver disease among the remaining six patients might be unconnected with alcohol. Mills and coworkers¹⁰ suggested that HBV infection might be a factor in those alcoholic patients who go on to develop chronic liver disease and cirrhosis. No difference was found in the prevalence of HBV markers in patients with alcoholic hepatitis and those with cirrhosis and a continuing alcoholic hepatitis. Further the prevalence of HBV markers in these two groups of patients was not significantly different from that in patients with steatosis. Thus the results of the present study do not seem to support the suggestion quoted above.

The problem of aetiology highlighted in the present study may be solved in prospective studies by the demonstration of HBV antigens in the liver tissue.

This study was supported by the Danish Medical Research Council (No 512-15529), Ebba Celinder's Foundation and Købmand i Odense Johann og Hanne Weimann f Seedorff's Foundation.

References

- ¹ Orrego H, Blendis LM, Blake JE, Kapur BM, Israel Y. Reliability of assessment of alcohol intake based on personal interviews in a liver clinic. *Lancet* 1979;ii:1354-6.
- ² Levin DM, Baker AL, Riddell RH, Rochman H, Boyer JL. Nonalcoholic liver disease. Overlooked causes of liver injury in patients with heavy alcohol consumption. *Am J Med* 1979;66:429-34.
- ³ Poulsen H, Christoffersen P. *Atlas of liver biopsies*. Copenhagen: Munksgård, 1979.
- ⁴ Hardt F, Aldershvile J, Dietrichson O, et al. Hepatitis B virus infections among Danish surgeons. *J Infect Dis* 1979;140:972-4.
- ⁵ Aldershvile J, Brock A, Dietrichson O, et al. Hepatitis B virus infections among Danish dentists. *J Infect Dis* 1978;137:63-6.
- ⁶ Skinhøj P, Olesen H, Cohn J, Mikkelsen M. Hepatitis-associated antigen in pregnant women. *Acta Pathol Microbiol Scand [B]* 1972;80:362-6.
- ⁷ Hawkes RA, Boughton CR, Schroeter DR, Decker RH, Overby LR. Hepatitis B infections in institutionalized Down's syndrome inmates: a longitudinal study with five hepatitis B virus markers. *Clin Exp Immunol* 1980;40:478-86.
- ⁸ London WT, DiFiglia M, Sutnik A, Blumberg BS. An epidemic of hepatitis in a chronic-haemodialysis unit. *N Engl J Med* 1969;281:571-8.
- ⁹ Torisu M, Yokoama T, Amemiya H, et al. Immunosuppression, liver injury and hepatitis in renal, hepatic, and cardiac homograft recipients: With particular reference to the Australia antigen. *Ann Surg* 1971;174:620-39.
- ¹⁰ Mills PR, Pennington TH, Kay P, MacSween RNM, Watkinson G. Hepatitis Bs antibody in alcoholic cirrhosis. *J Clin Pathol* 1979;32:778-82.

Requests for reprints to: M Orholm, M.D., 2nd Dept of Medicine, Københavns Kommunehospital, DK 1399 København K, Denmark.