Serological markers of hepatitis B in patients with alcoholic liver disease: a multi-centre survey

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SUMMARY In a study of 195 patients derived from five centres in northern Britain and with histologically confirmed alcoholic liver disease we have found an increased prevalence of serological markers of hepatitis B. This increased prevalence was found in each of the five centres; the overall frequency ranged from 11% sero-positivity in fatty liver, 12% in alcoholic hepatitis and 27% in cirrhosis.

In two previous studies from Glasgow, a significantly increased prevalence of hepatitis B virus (HBV) antibody was found in patients with alcoholic liver disease, in particular in patients with alcoholic cirrhosis.^{1,2} The reason(s) for this could not be established, and there was a possibility, albeit remote, that it might represent a local phenomenon peculiar to alcoholic liver disease in the west of Scotland. In the present study the prevalence of HBV markers has been examined in a series of 195 patients entering a survey of alcoholic liver disease in four cities in Scotland—Aberdeen, Dundee, Edinburgh and Glasgow, and one in the north of England—Newcastle-upon-Tyne.

Patients and methods

The patients, 151 men (mean age 51 yr, range 27-76) and 44 women (mean age 49 yr, range 23-72), all caucasian, were admitted to one of eight medical units co-operating in a survey of alcoholic liver disease funded by the Scottish Home and Health Department. A serum sample was obtained from each patient (in some more than one sample was examined) and was referred to the Regional Virus Laboratory, Ruchill Hospital, Glasgow for the HBV marker studies. The serum samples were coded and the results reported without prior knowledge of the histological diagnosis.

Each patient had a percutaneous needle biopsy of liver performed, and a histological diagnosis of alcohol-induced liver disease was established using routine staining methods. A distinction was made between active and inactive cirrhosis; in the former

features of alcoholic hepatitis³ were additionally present, whereas in the latter these were absent and evidence of liver cell necrosis was minimal.

Tests for hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs) and antibody to HB core antigen (anti-HBc) were carried out by standard radioimmunoassay methods (Ausria, II, Ausab and Corab—Abbott Laboratories) and reported as positive or negative compared with standard controls. Positive results for anti-HBs and anti-HBc were confirmed on repeated testing, and anti-HBs was only accepted as positive if the count was greater than five times the negative control mean, thus excluding any borderline results.

Results

The results obtained for each centre are summarised in Table 1. The prevalence of HBV markers ranges from 10% of alcoholic liver disease patients in Glasgow to 23% in Dundee, with an overall mean of 18%. Of the 36 patients in whom HBV markers were found 24 had both anti-HBs and anti-HBc, 2 had anti-HBc and HBsAg, 5 had anti-HBs alone, and 5 had anti-HBc alone.

The distribution of HBV markers according to the histological diagnosis is summarised in Table 2. This shows that the overall prevalence of HBV markers increases from 11% in patients with fatty liver to 30% in patients with inactive cirrhosis.

Discussion

In the present study we have found an increased prevalence of HBV markers in a series of patients with histologically documented alcoholic liver

Table 1 *Distribution of patients and markers of HBV infection in different centres. Percentages of total numbers per centre are shown in brackets*

	Total No	Hepatitis B virus markers				Total with at least one marker
		HBsAg	anti-HBc alone	anti-HBs alone	Both anti-HBc and anti-HBs	
Aberdeen	21— 6 F*	0	—	—	3	3(14)
Dundee	40—10 F	1†	—	1	7	9(23)—2 F
Edinburgh	50—15 F	1†	3	2	4	10(20)—1 F
Glasgow	42— 9 F	0	1	—	3	4(10)—1 F
Newcastle	42— 4 F	—	1	2	7	10(24)—1 F

*F = female.

†These were also positive for anti-HBc.

Table 2 *Distribution of markers of HBV infection according to the histological diagnosis of alcoholic liver disease. Percentages are shown in brackets*

	Total No	Hepatitis B virus markers				Total with at least one marker
		HBsAg	anti-HBc alone	anti-HBs alone	Both anti-HBc and anti-HBs	
Fatty liver	62—10 F*	—	1	2	4	7(11)—1 F
Alcoholic hepatitis	43—14 F	—	1	—	4	5(12)—1 F
Alcoholic cirrhosis						
active	80—19 F	2†	2	3	14	21(26)—3 F
inactive	10— 1 F	—	1	—	2	3(30)
Totals	195—44 F	2(1)	5(3)	5(3)	24(12)	36(18)—5 F

*F = female.

†These were both positive for anti-HBc.

disease, derived from five different centres in northern Britain. This confirms the earlier observations made by Mills and his colleagues in Glasgow.^{1,2} In previous studies using radioimmunoassay techniques identical to or of equal sensitivity to those used in the present study, the frequency of HB surface antigenaemia in the general population in the west and east of Scotland was 1 in 84¹⁴ and 1 in 77¹⁵ respectively, and this compares with 2 of 195 in our series of alcoholic-liver disease patients; the frequency of anti-HBs in the west and east of Scotland was 2.2%⁶ and 2.9%⁷ respectively, findings which compare with an overall 15% positive rate in the present study. It is thus apparent that in five centres in northern Britain there is good evidence of an association between alcoholic liver disease and HBV infection.

Buffet and his colleagues (personal communication) in a study of 27 French patients with alcoholic liver disease found anti-HBs and anti-HBc in 10 (37%) and 13 (47%) patients respectively. In a recently reported prospective study from the alcohol treatment unit of the Brockton VA Medical Centre in Boston, Chopra and his colleagues⁸ found an overall prevalence of HBV infection of 25.5% in a series of 90 consecutive patients admitted to the unit. The

sera of these patients were screened for HBsAg (1.1% positive), anti-HBs (24%) and anti-HBc (19%), but the authors do not indicate whether there was any clinical evidence of liver disease in the patients, nor did they study a control group. These reports however, provide further evidence of a possible association between alcoholic liver disease and HBV infection.

Mills and his colleagues^{1,2} were not able to offer an explanation for the increased prevalence of HBV infection in alcoholic liver disease. Factors such as social class, age and previous history of possible exposure by blood transfusion, tattooing etc were excluded by these workers. We are similarly not able to offer an explanation for the present findings. The increased risk of HBV infection among male homosexuals is now well documented.⁹⁻¹¹ We have no record of the sexual orientation of the patients currently studied, but we do not think that this is the likely explanation for our findings.

In the patients who were sero-positive for HBV markers there was no clinical indication as to when they had acquired this infection. Of the 36 sero-positive patients 24 were found to have both anti-HBs and anti-HBc, an antibody profile indicating recovery from the hepatitis episode with elimination

of the virus and the development of an immune state. In 7 patients anti-HBc but no anti-HBs was demonstrated, and in 2 of these HBsAg was also found. The failure of these 7 patients to produce anti-HBs suggests a possible carrier state and they will be the subject of continued follow-up.

Our results also show an increased prevalence of HBV infection in fatty liver, the mildest form of alcoholic liver disease, but the highest incidence occurred in patients with cirrhosis. It is noteworthy that a 26% prevalence of HBV markers has been found in patients with active alcoholic cirrhosis. In the biopsies from these patients features of alcoholic hepatitis were also present, and thus the assumption must be that the cirrhosis was alcohol-induced. In contrast, in the 10 patients with inactive cirrhosis, and in whom HBV markers were found in 3 (30%), stigmata of alcoholic liver disease were absent, and the possibility cannot be excluded that, in these patients, the cirrhosis occurred with alcoholism but was of a different aetiology. We have no evidence, however, in any of the patients studied, that the HBV infection contributed to the liver injury, although the possibility cannot at present be excluded.

The findings reported in this paper suggest that there is an increased susceptibility to HBV infection in patients with alcoholic liver disease and these patients may represent an important source of HBV infection in the community.

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