Hepatitis B Virus Prevalence in a Liver Biopsy Series in Jeddah, Saudi Arabia

P. E. Coode, J. Hossain, M. B. Ibrahim


Liver biopsies from 228 patients, in Jeddah, Saudi Arabia, were retrospectively reviewed. Autoimmune liver disease and alcoholic cirrhosis are rare in this community, an observation confirmed in this series. For both the chronic active hepatitis and the cirrhosis cases, 20% had evidence of chronic hepatitis B infection. In a population known to have a chronic hepatitis B carrier prevalence of about 7%, this figure was unexpectedly low, though the findings are in accord with some other published series. There have been significant variations in different reports. For the hepatocellular carcinoma cases 62% were hepatitis B surface antigen positive. In many cases of serious chronic liver disease in this community, the aetiology remains unknown.

Liver disease is an important cause of morbidity and mortality in the Middle East, but accurate information regarding its pattern and prevalence is still lacking. This is particularly the case in an area where in general there is no formal system of death certification. A series of consecutive liver biopsies from a hospital in Jeddah, was examined to establish the pattern of chronic liver disease with particular reference to the patients' hepatitis B status.

Subjects and Methods

All the liver biopsies performed at King Khalid National Guard Hospital (KKNGH), Jeddah, were examined. The hospital first started taking patients in 1984, and all the biopsies on file to August 1990 were assessed. (Patients include National Guard servicemen, and their extended families, together with civilians.) Fifteen patients of non-Arabic nationality were excluded, as well as 30 cases in which the biopsy was inadequate. This left 245 biopsies. Seventeen patients had had more than one 'adequate' biopsy: for these only the most pertinent biopsy was recorded. This gave a total of 228 biopsies, in 228 patients. There were 161 needle biopsies (Trucut type), 50 wedge biopsies, and 17 fine needle aspirations (FNA).

The slides were reviewed, with the original history reports and the clinical case records. Hepatitis B surface antigen (HBsAg) was assayed using monoclonal enzyme immunoassay kits (Abbott, Auszyme). Most patients had at least two tests, at an interval of more than 6 months. Autoimmune profiles, for anti-nuclear antibody (ANA) and a range of autoimmune antibodies, including antimitochondrial and anti-smooth muscle antibodies, were read using standard immunofluorescence techniques.
Table 1
Liver biopsy disease categories

<table>
<thead>
<tr>
<th></th>
<th>Saudi</th>
<th>Yemeni</th>
<th>Other Arabic</th>
<th>Total lesions</th>
<th>Total as %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>25</td>
<td>6</td>
<td>3</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>Fatty change</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>N-S reactive hepatitis</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Chronic active hepatitis</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>32</td>
<td>5</td>
<td>7</td>
<td>44</td>
<td>19</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>34</td>
<td>3</td>
<td>2</td>
<td>39</td>
<td>17</td>
</tr>
<tr>
<td>Other malignant cases</td>
<td>19</td>
<td>4</td>
<td>1</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>35</td>
<td>8</td>
<td>3</td>
<td>46</td>
<td>20</td>
</tr>
<tr>
<td>Total patients by nationality</td>
<td>181</td>
<td>28</td>
<td>19</td>
<td>228</td>
<td>100</td>
</tr>
</tbody>
</table>

NS: Non-specific.

Table 2
Cirrhosis by type

<table>
<thead>
<tr>
<th>Cirrhosis</th>
<th>No. of cases</th>
<th>HBsAg positive</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Micronodular</td>
<td>28</td>
<td>6 (21%)</td>
<td>10</td>
</tr>
<tr>
<td>Macronodular</td>
<td>13</td>
<td>3 (23%)</td>
<td>8</td>
</tr>
<tr>
<td>Incomplete septal</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>44</td>
<td>9 (20%)</td>
<td></td>
</tr>
</tbody>
</table>

Chronic active hepatitis (CAH) was classified as mild, moderate, or severe. Most cases of cirrhosis show inflammation of the septal areas, and in some piecemeal necrosis; this inflammatory component was also graded. (Other approaches to classification have been used, and this may contribute to differences noted in comparing series.) Differentiation between micro- and macronodular cirrhosis was based principally on whether the nodules were multi-acinar, rather than on nodule size.

Results

Of the 228 patients, 181 were Saudis, and 47 were from neighbouring Arabic countries, including 28 Yemenis. One hundred and thirty patients were male, and 98 were female. The average age was 46 years. The main disease categories are listed in Table 1.

Two patients had chronic persistent hepatitis (CPH). There were 10 cases of chronic active hepatitis (CAH) (seven men and three women: average age 47 years). Two were graded as mild, and eight as severe.

Forty-four cases of cirrhosis were recorded (25 men and 19 women: average age 48 years) (Table 2). Almost three quarters of the cases reported as 'macronodular cirrhosis' were diagnosed in wedge biopsies (rather than in needle biopsies) as were all three cases of incomplete septal cirrhosis. In contrast only one in five of the ‘micronodular cirrhosis’ cases was diagnosed in the wedge biopsies.

Among the 39 cases of hepatocellular carcinoma, there were 31 males and 8 females (M:F ratio 4:1) with an average age of 62 years. Eight were diagnosed by FNA.

The remaining biopsies encompassed a wide range of conditions. Fatty change, which was present in 8%, was only recorded when of moderate or severe degree. Thirteen biopsies were reported as 'non-specific reactive hepatitis'. There were nine cases of granulomatous hepatitis, six of unknown aetiology, two of tuberculosis, and one of sarcoidosis. There was a single case of alcoholic hepatitis. Three patients had schistosomal portal fibrosis (all non-Saudis). There was one case of primary cholangiocarcinoma, and 23 cases of metastatic tumours.

Hepatitis B surface antigen status

This was recorded in 219 cases, that is in all but nine patients. There were in total 46 positive cases, 37 men and nine women (average age 53 years—only two patients were aged less than 10 years). The HBsAg status for selected disease categories is listed in Table 3. The information for other hepatitis markers was incomplete. In the cirrhotic group, 12 of the HBsAg negative cases had been tested for surface (anti-HBs) and core (anti-HBc) antibodies. Five patients had anti-HBs indicating previous infection, and two had anti-HBc alone, possibly indicating hepatitis B virus (HBV) replication. The remaining five had neither antibody. An autoimmune profile was performed in 46 patients. Clinicians tend to have reserved the test for otherwise unexplained disease. (Only one of these cases was known to be HBsAg positive.) One patient, a Yemeni female aged 27, with an ANA titre of 1:1280, and weakly positive anti-smooth muscle antibodies, had previously been diagnosed as CAH, confirmed by biopsy. A repeat biopsy, included in this series,
Table 3
Hepatitis B status, by disease category

<table>
<thead>
<tr>
<th></th>
<th>Normal and fatty change</th>
<th>N-S reactive hepatitis</th>
<th>CAH</th>
<th>Cirrhosis</th>
<th>Hepato-cellular carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number in series</td>
<td>52</td>
<td>13</td>
<td>10</td>
<td>44</td>
<td>39</td>
</tr>
<tr>
<td>HBsAg not done</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>HBsAg positive</td>
<td>0</td>
<td>4</td>
<td>2 (20%)</td>
<td>9 (20%)</td>
<td>24 (62%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CAH: Chronic active hepatitis; N-S: Non-specific.

showed only chronic persistent hepatitis—the patient was taking steroids. This was the only case of autoimmune CAH. No case of primary biliary cirrhosis was recorded. Eleven patients had a range of weakly positive antibodies, considered to be non-specific. There were two patients with documented SLE, with only minimal liver biopsy abnormalities.

Discussion

The proportion of patients having CPH and CAH was unexpectedly small in comparison with the number of cases of cirrhosis, through this is in keeping with some previous reports.5,7,8 By implication, many patients with chronic liver disease are presenting late. This has been noted before, and a more active approach to screening has been encouraged.9

Also unexpected was the large proportion of macronodular cirrhosis cases diagnosed in wedge biopsies. This differences can be partly explained by interpretational bias, but it probably also represents a different level of disease activity in the two groups. About half of the wedge biopsies were taken incidentally during laparotomy because the liver appeared abnormal: the remainder were taken during surgery for portal hypertension.

There is a marked regional variation in schistosomiasis in Saudi Arabia—the rate is low in this series, with only three cases of schistosomal hepatic fibrosis, none of whom were Saudis. (In our experience the pattern of fibrosis is distinctive, and it should not cause diagnostic confusion.10)

Regional variations in hepatitis B carrier rates, usually assessed in blood donors, have been well documented in Saudi Arabia, though many epidemiological studies have been influenced by the inclusion of non-Saudis. HBsAg prevalence varies from 4.7% in the Riyadh to 19.9% in Gizan.11-14 A high rate for hepatitis delta virus carriers has been documented.15 Of 19724 blood donors in this hospital (KKNGH) recently examined, 19210 were male, and of these 1418 were HBsAg positive, giving a prevalence in men of 7.4%.

In the present study, for both the CAH and cirrhosis cases, the proportion with hepatitis B surface antigenaemia was the same at one in five (20%). Given the high prevalence of hepatitis B in Saudi Arabia this figure seems unexpectedly low. In a report from Riyadh, hepatitis B surface antigenaemia was recorded in 'only' 14% of patients having liver biopsies, but there was no analysis by disease category.7 In the series from the King Abdulaziz University Hospital, Jeddah,8 the hepatitis B data was incomplete, but interestingly of five cases of cirrhosis tested only one was HBsAg positive.

In a recent Riyadh study, eight of 18 patients with CAH (44%), and 11 of 28 cases of cirrhosis (39%), were HBsAg serum positive.16 From the King Faisal Specialist Hospital, Riyadh, in 100 cases of chronic active hepatitis, 51% were HbsAg positive.4 This result, higher than for other Saudi series, may be explained by patient selection. In a Kuwaiti study, using immunohistochemical examination of liver biopsy sections, HbsAg was found in 29% of CAH, and 27% of cirrhotic liver biopsies.5 In the UK with a prevalence HBV antigaenaemia of less than 0.5%, HbsAg was demonstrated in 10% of patients with CAH and cirrhosis.17

Of the hepatocellular carcinomas in the present series, 62% were HbsAg positive. In Riyadh 55%, and in Dammam 46%, were positive.18,19

It is noteworthy that none of the cases that were reported as normal, or as having fatty change, tested positive for HbsAg (Table 3).

Our knowledge of viral hepatitis has been greatly enhanced by the use of molecular techniques. Chronic HBV infection can be divided into three serological categories:20

(1) HBsAg positive, HBeAg positive, HBV-DNA positive,
(2) HBsAg positive, HBeAg negative, HBV-DNA positive,
(3) HBsAg positive, HBeAg negative, HBV-DNA negative.

This has important implications for prognosis.20 The second group has been attributed to a specific virus mutant21—this group is small, but epidemiological studies are incomplete.

The role of hepatitis C in chronic liver disease and hepatocellular carcinoma is now well documented.20 In a survey in Riyadh 1.5% of
blood donors have been reported to have anti-HCV antibodies. In a recent Riyadh study, five of 18 patients with CAH (28%), eight of 28 cirrhotics (29%) and 11 of 42 cases of hepatocellular carcinoma (26%), had HCV antibodies. To provide necessary epidemiological data, all patients having liver biopsies should be examined for all appropriate hepatitis markers. It should not be forgotten that infection with the delta virus, as well as HCV, may co-exist with hepatitis B. While hepatitis B and C between them apparently account for most cases of serious chronic liver disease in Saudi Arabia, many cases are still unexplained.

Acknowledgements

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References