Significance of hepatitis B virus antibodies in Saudi patients with chronic hepatitis C infection.

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ABSTRACT
Objectives: To study the clinical significance of antibodies to hepatitis B virus among 100 Saudi patients with chronic hepatitis C virus infection.

Subjects: The records of 100 patients with hepatitis C virus (HCV) infection who were admitted between November 1990 and January 1994 were retrospectively studied. These patients were classified into 3 groups according to their serological hepatitis B virus (HBV) status. Group I comprised of 43 patients lacking in HBV antibody and serving as controls. Twenty-nine patients in Group II were positive for HBCAb only, while Group III included 28 patients positive for both HBCAb and HBsAb.

Results: Patients with hepatitis C infection who had hepatitis B core antibodies (HBCAb) or both HBCAb and hepatitis B surface antibodies (ABsAb) were more likely to be cirrhotic as compared to sex and age, matched controls lacking antibodies to HBV (75.8% and 80% respectively vs 48.5%). When present, cirrhosis was more likely to be decompensated in patients with HBV antibodies as compared to controls (36% and 37.5%) vs 0% Child-Pugh’s grade C. Number of hepatocellular carcinomas (HCC) appeared to be related to that of cirrhosis (28% and 34% vs 31% in controls).

Conclusions: It is concluded that patients with chronic hepatitis C virus infection have more severe liver disease when they have been previously infected by hepatitis B virus.

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Keywords: Hepatitis B, hepatitis C, liver cirrhosis, hepatocellular carcinoma.

Hepatitis B and C viruses share several modes of transmission, implying that co-infection with both viruses might occur frequently.\(^1\)\(^2\)\(^3\) Co-infection with both viruses (HBV and HCV) will result in more severe liver disease.\(^4\)\(^5\) Liver diseases due to hepatitis B virus or hepatitis C virus are common in Saudi Arabia.\(^6\)\(^7\) This study assess the clinical significance of antibodies to hepatitis B virus in 100 Saudi patients with chronic hepatitis C virus infection.

Patients and methods Records of 140 patients with chronic hepatitis C virus infection admitted between November 1990 and January 1994 to the Armed Forces Hospital, Riyadh, Saudi Arabia were retrospectively reviewed. This study included patients who had: (1) HCV antibodies (anti HVC); (2) screening for hepatitis B virus (HBV) makers; (3) availability of a histology diagnosis and (4) sex and age (+ 1 year) matched to compare different groups. Patients admitted to the hospital more than once within the period studied were included only once in the study (first admission). Patients with HBsAg positive and treated with antiviral drugs, were excluded from the study. None of the patients were HIV 1 or HIV 2 positive.

One hundred patients fulfilled the inclusion criteria. These patients were classified in 3 groups according to their serological HBV status. Group I comprised 43 patients lacking in HBV antibody and serving as controls. Twenty-nine patients in Group II were positive for HBCAb only while Group III included 28 patients positive for both HBCAb and HBsAb. Anti HCV was assayed by means of second generation ELISA (Ortho Diagnostic Systems, Racitan, NJ) and confirmed with recombinant immunoblot assay (RIBA 2, Chiron Corporation, Emeryville, CA). HBV markers were determined using immunoassays and HIV using ELISA (Abbott Laboratories, North Chicago, IL). Routine serum biochemical tests were carried out by means of automated techniques (SMAC, Techtron). Histopathological findings of liver biopsies were graded as non-specific, chronic persistent hepatitis (CPH), chronic active hepatitis (CAH) or cirrhosis using standard criteria. When indicated (space...
Table 1 - Clinical findings

<table>
<thead>
<tr>
<th>Findings</th>
<th>No of patients</th>
<th>(%)</th>
<th>No of patients</th>
<th>(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>5</td>
<td>(15.2)</td>
<td>12</td>
<td>(60)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Jaundice</td>
<td>1</td>
<td>(3.0)</td>
<td>7</td>
<td>(35)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>GI bleed</td>
<td>1</td>
<td>(3.0)</td>
<td>6</td>
<td>(30)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>1</td>
<td>(3)</td>
<td>6</td>
<td>(30)</td>
<td>&lt;0.01</td>
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</tbody>
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The number of HCC appeared to be significantly higher in patients with HBCAb and HBsAb as compared to controls (p<0.01). However, when the number of HCC considered relative to the number of cirrhosis, no difference could be observed among the groups of patients HBV antibody positive with regard to the number of cirrhosis (Child-Pugh class C cirrhosis) or that of HCC relative to cirrhosis.

Discussion The present study indicates that liver disease is more severe in Saudi patients positive for concurrent HCV and HBV antibodies than in controls with anti HCV alone, both clinically and histologically. This is in agreement with the previous observation in patients co-infected with both HCV and HBV.4,5 We therefore suggest that HCV and HBV antibodies found concomitantly might indicate recent or past co-infection with both viruses. Hepatitis C virus would then inhibit the replication of HBV resulting finally in HBsAg clearance as suggested by others.4,5,9 In support of this hypothesis is the fact that 30 (40%) out of 73 patients with positive HBV antibodies were known to have chronic liver disease 2-7 years before they were enrolled in the present study. These patients exhibited altered transaminase activity after HBsAg clearance, which is ascribed to non-A, non-B generally or HCV.9,11 Accordingly, anti HCV could be shown in these

Table 2 - Histological findings in the three groups.

<table>
<thead>
<tr>
<th>Histological findings</th>
<th>No of patients</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Group 1</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>20</td>
</tr>
<tr>
<td>CAH</td>
<td>15</td>
</tr>
<tr>
<td>Non specific</td>
<td>4</td>
</tr>
<tr>
<td>CPH</td>
<td>1</td>
</tr>
<tr>
<td>HCC</td>
<td>3</td>
</tr>
</tbody>
</table>
patients when HCV screening tests become available. Moreover, direct evidence of HbsAg clearance could be provided by the eventual observations of 6 patients shown to be co-infected with HCV and HBV. Two of these patients converted to HbcAb after HbsAg clearance while the others became positive for both HbcAb and HbsAb without any change in the clinical state of their liver disease. It is unclear why seroconversion thus reverted to HbcAb or rather HbcAb and HbsAb. The latter observation might account for the lack of statistical difference we noticed when we compared patients positive for anti-HCV and HbcAb to those with anti-HCV, HbcAb and HbsAb. Chronic liver disease in both HBV and HCV may progress to cirrhosis and eventually to hepatocellular carcinoma. The mode of carcinogenesis is uncertain. However, the essential end result for HBV seems to be rearrangement of hepatocyte DNA. In contrast HCV carcinogenesis might be through cirrhosis. In the present study, HCC appeared to be closely related to cirrhosis. Approximately 30% of cirrhosis were complicated by HCC irrespective of the group considered.

Conclusion Our patients with concurrent HCV and HBV antibodies probably have a past history of co-infection with both viruses. Accordingly, dual infection with HCV and HBV might be a frequent event in this region. This is of importance since co-infection with these viruses appears to result in more severe liver disease.

References

10. Liaw YF, Lin SM, Sheen IS, Chu CM. Acute hepatitis B virus superinfection followed by spontaneous HBsAg seroconversion and HbsAg elimination. Infection (German) 1994; 250-251.