Comparison of the Histological and Serological Parameters of Patients with Hepatitis Delta Virus in Active and Inactive Hepatitis B Virus Carriers

Samiullah Shaikh¹, Devrajani Bikha Ram¹, Shaikh Tanveer² and Asra Talpur¹

ABSTRACT

Objective: To assess the histological and serological parameters of patients with hepatitis delta virus (HDV) in active HBV versus inactive HBV carriers.

Study Design: An observational study.

Place and Duration of Study: Medical Unit IV at Liaquat University Hospital, Jamshoro, Sindh, from June 2008 to September 2011.

Methodology: This study included 49 consecutive inactive HBV carriers who were HBsAg-positive, HBV DNA-negative, anti-D antibody-positive, and HDV RNA-positive, as well as 277 patients with active HBV who were HBsAg-positive, anti-HDV antibody-positive, HDV RNA-positive, and demonstrated > 20,000 IU/mL HBV DNA and > 2 (ULN) serum glutamic pyruvic transaminase (SGPT). Informed consent was obtained from each patient. Liver biopsies were obtained and the staging of fibrosis was performed according to the METAVIR scoring system. Continuous variables such as age, SGPT, platelet count, and the HBV DNA level were computed as the mean ± standard deviation. Categorical variables such as gender and stage of fibrosis are expressed as percentages. All data were processed using SPSS version 16.

Results: This study included 49 patients in an inactive HBV group. Fibrosis stage 0 was observed in 37 (75.5%) patients and 12 (24.5%) were stage 1. Among the 277 patients with active disease, fibrosis stage 0 was present in 7 (2.5%) patients, stage 1 in 31 (11.2%) patients, stage 2 in 172 (62.1%) patients, stage 3 in 44 (15.9%) patients and stage 4 in 23 (8.3%) patients.

Conclusion: HDV in active HBV carriers is severe on its initial presentation and requires prompt treatment whereas in inactive HBV carriers demonstrates an indolent course.

Key Words: Hepatitis D. Asymptomatic carriers. Fibrosis.
METHODOLOGY

This observational study was conducted in Medical Unit-I at Liaquat University Hospital, Jamshoro, Sindh, Pakistan from June 2008 through September 2011. The study included 49 consecutive inactive HBV carriers who were HBsAg-positive, HBV DNA-negative, anti-D antibody-positive, and HDV RNA-positive, as well as 277 patients with active HBV who were HBsAg-positive, anti-HDV antibody-positive, HDV RNA-positive, detectable HBV DNA and > 2 (ULN) serum glutamic pyruvic transaminase (SGPT). Informed consent was obtained from each patient. The study was performed according to the ethical guidelines of the 1975 Declaration of Helsinki. All patients were part of the Hepatitis Prevention and Control Program, Sindh Chief Minister’s Initiative, Sindh, Pakistan.

The following exclusion criteria were applied: an age of < 18 or > 65 years; pregnant women or nursing mothers; concomitant HCV infection; decompensated cirrhosis of the liver (e.g., history of ascites, variceal bleeding, or hepatic encephalopathy); metabolic liver disease (such as Wilson’s disease or hemochromatosis); leukopenia (< 2500 cells/mm³); neutropenia (< 1000 cells/mm³); haemoglobin < 10 g/dL; other severe diseases (e.g., cardiomyopathy, diabetes mellitus, arterial hypertension, neoplasia, neurologic diseases); depression, and/or psychiatric disorders, alcoholics.

Patients were diagnosed with HDV based on the presence of anti-HDV antibodies and HDV RNA in the serum. Patients were diagnosed as active carriers if they were positive for HbAgs and demonstrated detectable HBV DNA levels with or without positivity for the HBe antigen. Patients were diagnosed as an inactive HBV carrier if they were HBsAg-positive, HBe antigen negative, Anti-HBe antibody positive, and HBV DNA negative. Routine serological tests, such as a complete blood count, liver function test, prothrombin time, alanine aminotransferase (ALT), serum albumin, anti-HDV antibodies, HbAgs, and abdominal ultrasound, were performed at the research laboratory of Liaquat University of Medical and Health Sciences, Jamshoro. HDV RNA and HBV DNA analyses were performed at the molecular laboratory of Liaquat University of Medical and Health Sciences, Jamshoro. Liver biopsies were performed on all patients by a trained professional after obtaining written consent and fully explaining the procedure to each patient. The procedure was performed under ultrasound guidance using a 14-gaugetru-cut biopsy needle. All patients tolerated the procedure well without developing any major complications such as haemorrhage and blood transfusion, prolonged pain, haematoma formation, shock, or biliary peritonitis. The biopsy sample was considered adequate if it was > 10 mm in size and contained > 5 portal tracts. Each biopsy was sent to a pathologist who was blind to

RESULTS

The cohort study included 49 patients in an inactive HBV group. The mean age was 29.3 ± 7.4 years, the mean haemoglobin level was 11.74 ± 2.75 g/dl, the mean platelet count was 300.11 x 10³ ± 21.34 and the mean SGPT level was 20.8 ± 7.98 IU/L. Of these 49 patients, 33 (67.3%) were males and 16 (32.7%) were females. Fibrosis stage 0 was indicated in 37 (75.5%) of these cases and 12 (24.5%) further cases were classified as stage 1.

Among the 277 patients with active HBV group, the mean age was 29.7 ± 8 years, the mean haemoglobin level was 12.65 ± 2.3 g/dl, the mean platelet count was 169.02 ± 15.93 x 10³, the mean SGPT level was 124.4 ± 28.2 IU/L, and the mean HBV DNA level was 139.22 x 10³ ± 37 IU/mL. Of these 277 patients, 210 (75.80%) were males and 67 (24.2%) females. Fibrosis stage 0 was indicated in 7 (2.5%) patients, stage 1 in 31 (11.2%) patients, stage 2 in 172 (62.1%) patients, stage 3 in 44 (15.9%) patients, and stage 4 in 23 (8.3%) patients. Table I describes the baseline characteristics of the patients.

Table I: Baseline characteristics of the patients analyzed in this study.

<table>
<thead>
<tr>
<th>Continuous variable</th>
<th>Inactive HBV carriers (n = 49)</th>
<th>Active HBV carriers (n = 277)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>29.3 ± 7.4</td>
<td>29.7 ± 8</td>
</tr>
<tr>
<td>Hemoglobin (g/dL), mean ± SD</td>
<td>11.74 ± 2.75</td>
<td>12.65 ± 2.3</td>
</tr>
<tr>
<td>Mean platelet count (10³/mm³), mean ± SD</td>
<td>300.11 ± 21.34</td>
<td>169.02 ± 15.93</td>
</tr>
<tr>
<td>SGPT (IU/L), mean ±SD</td>
<td>20.8 ± 7.98</td>
<td>124.4 ± 28.2</td>
</tr>
<tr>
<td>HBV DNA level (IU/mL), mean ±SD</td>
<td>Nil</td>
<td>139.22 x 10³ ± 37</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Categorical variable</th>
<th>Frequency / percentage</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Male</td>
<td>33 (67.3%)</td>
<td>210 (75.80%) Female</td>
</tr>
<tr>
<td>Stage of fibrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 0</td>
<td>37 (75.5%)</td>
<td>7 (2.5%)</td>
</tr>
<tr>
<td>Stage 1</td>
<td>12 (24.5%)</td>
<td>31 (11.2%)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>0 (0)</td>
<td>172 (62.1%)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>0 (0)</td>
<td>44 (15.9%)</td>
</tr>
<tr>
<td>Stage 4</td>
<td>0 (0)</td>
<td>23 (8.3%)</td>
</tr>
</tbody>
</table>

SGPT = Serum Glutamic Pyruvic Transaminase; HBV = Hepatitis B virus.
DISCUSSION

In this study, which included 49 asymptomatic HBV carriers, fibrosis stage 0 was diagnosed in 37 (75.5%) patients and stage 1 was diagnosed in 12 (24.5%) patients. There is no previously reported data for patients with HDV in inactive HBV carriers. In 1978, Velasco et al. performed liver biopsies on 19 inactive carriers and found a normal histology in 18 patients with one patient diagnosed with stage I fibrosis.10 According to de Franchis et al., who performed biopsies on 88 inactive carriers, mild hepatitis (stage I fibrosis) was found in 3 (3.4%) patients; the remaining 85 carriers were diagnosed with stage 0 fibrosis.12 In another French study, liver biopsies were conducted on 85 inactive carriers: 80 (91%) cases were diagnosed with stage 0 fibrosis and 5 (9%) were diagnosed with stage I fibrosis. One of the most important previous findings was observed by Zacharakis et al., who followed asymptomatic carriers for 4 years using follow-up biopsies after performing baseline evaluations. These researchers found no evidence of fibrosis at baseline that persisted during the follow-up biopsies.13 In contrast to these studies, a higher proportion of histologically active disease was reported in asymptomatic carriers in a Korean study of 110 asymptomatic carriers, of which approximately 49% of patients demonstrated some pathology on liver biopsy (31% chronic persistent hepatitis, 11% chronic active hepatitis, and 7% cirrhosis).14

In the present study of 277 patients with active HBV, fibrosis stage 0 was present in 7 (2.5%) patients, stage 1 in 31 (11.2%) patients, stage 2 in 172 (62.1%) patients, stage 3 in 44 (15.9%) patients, and stage 4 in 23 (8.3%) patients. In a previous report from Castelnau et al. on 14 patients, fibrosis stage 2-3 was observed in 10 (71.4%) patients and 4 (28.5%) patients demonstrated cirrhosis (stage 4) according to the METAVIR scoring system.15 Niro et al., in a study of 16 patients, observed stage 2-3 fibrosis in 4 (25%) patients, whereas 12 (75%) patients demonstrated stage 4 fibrosis.16 Wedemeyer et al., in a Hep-Net-International Delta Hepatitis Intervention Trial (HIDIT) trial (the largest multicentre trial conducted on HDV so far), recruited 90 patients. They observed stage 4 fibrosis in 6 (6.6%) patients, whereas the remaining 84 (93.4%) of patients demonstrated stage 2-3 fibrosis.17

This study showed absence of HBV DNA levels in inactive HBV carriers. Zacharakis et al.13 in their study of 263 compared HBV-DNA levels in different groups of HBV patients. A persistent low levels of HBV-DNA (<2000 IU/ml) was found in inactive carriers during 12 years follow-up. A constant low levels of HBV-DNA levels (<2000 IU/ml) was found at the baseline and during the largest follow-up so far of 30 years in Italian inactive carriers blood donors.18

Chu et al. in their cohort study found HBV-DNA levels < 20.6 IU/ml (103 copies/ml) in 58% of inactive carriers. 36% had 20.8 IU/ml (104 copies/ml) and 10% had > 21 (105 copies/ml) IU/ml. Non of these inactive carriers in cohort had HBV-DNA levels > 21.2 IU/ml (106 copies/ml).19

In this study, the mean DNA level in HBV active carriers was 139.22 x 10^3 ± 77.5 IU/ml. Niro et al. in their study of 61 patients found higher than 20,000 IU/ml level of HBV-DNA in 50 patients.20 Wedemeyer et al., recruited 90 patients in HIDIT trial. Median baseline HBV-DNA was 1.38 log<sup>10</sup> copies/ml in PEG-INFα-2a plus Adefovir group, 2.57 log<sup>10</sup> copies/ml in PEG-INFα-2a plus placebo group and 2.08 log<sup>10</sup> copies/ml in Adefovir group.17

The mean SGPT levels was 20.8 ± 7.98 IU/L in this study of 49 asymptomatic carriers. Tai et al. during the 10 years follow-up of 477 HBV inactive Taiwanese carriers with persistently normal SGPT found that only 0.7 – 0.9% patients developed cirrhosis.21 In another study from India consisting of 217 asymptomatic HBV carriers with persistently normal SGPT showed SGPT flares in 43 patients during the mean follow-up of 69 months.22 Yuen et al., found no flare-up in their 3233 Chinese patients with normal SGPT levels followed for a mean of 47 months.23 It is important to know that HBV inactive carriers with HDV also behaves same as inactive carriers alone and needs further follow-up as there is no such study with HBV inactive carriers with HDV.

The mean SGPT level was 124.4 ± 28.2 IU/L in active HBV carriers with HDV in the present study. Taghavi and colleagues observed that patients with significantly higher level of SGPT had significant fibrosis than HDV negative patients.24 In another study from China patients observed serious chronic hepatitis, severe hepatitis and liver cirrhosis with high SGPT.25

CONCLUSION

HDV in asymptomatic healthy carriers demonstrates an indolent course; therefore, regular follow-up examinations are needed at infrequent intervals. On the other hand, HDV in active HBV carriers is severe on its initial presentation and requires prompt treatment.

REFERENCES


