Original Article

Study on seroprevalence of hepatitis delta in a regional hospital in western Turkey

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Abstract

Introduction: Hepatitis delta virus (HDV) is an incomplete virus dependent on hepatitis B virus (HBV) for its multiplication. It can infect individuals with active HBV infection and cause severe liver disease. It is less prevalent than hepatitis B virus, but it causes more serious clinical pictures. In this study we investigated anti-HDV seroprevalence and epidemiological features among HBsAg seropositive outclinic patients at Izmir Tepecik Educational and Research Hospital.

Methodology: Serum samples collected from outpatients at Izmir Tepecik Educational and Research Hospital between 1 September 2007 and 30 August 2009 were evaluated. Anti-HDV assay was performed by enzyme immunoassay (EIA). Patients over the age of fourteen who were referred to our hospital were taken into the study.

Results: Out of 3,094 HBsAg positive patients, 79 (2.5%) had anti-HDV IgG seroprevalence. Of these 79 patients, 42 were hepatitis B carriers, 34 had chronic hepatitis B, two had liver cirrhosis, and one had hepatocellular carcinoma.

Conclusion: Although superinfection and co-infection of HDV are less prevalent than hepatitis B infection, the prognosis is worse as the response to therapy is poor; therefore, patients with hepatitis B should be evaluated further for HDV infection.

Key words: delta hepatitis; seroprevalence; hepatitis B infection


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Introduction

Hepatitis D virus infection is a worldwide health problem and the cause of liver-related morbidity and mortality. It is a defective RNA virus depending on HBV for replication and expression [1]. Hepatitis delta virus (HDV), which is a defective virus, was first investigated in 1977 [1]. HDV spread rapidly and became an important risk factor for patients with hepatitis B infection. Although it is less prevalent than hepatitis B virus (HBV), HDV deserves attention because of its association with a complicated clinical picture. Globally, more than 350 million people have developed chronic HBV infection, causing one million HBV-related deaths each year [2-4]. Turkey is in the middle endemic region. Epidemiological studies conducted in eastern and southeastern Anatolia of our country indicated 20% delta hepatitis superinfection among hepatitis B infected patients. These data indicate that delta hepatitis is an important issue in our country [5].

HDV is a defective RNA virus. The RNA genome is the smallest among human hepatitis viridae and contains 1,700 base pairs. The surface proteins of HDV are produced by HBV surface antigen. According to sequence analysis, the virus has three different genotypes. HDV, also known as hepatitis delta virus, is a defective RNA virus that requires HBV for its virion assembly and penetration into hepatocytes. There are three genotypes of HDV, identified on the basis of analysis of HDV genomes from various parts of the world. Genotype I is the most prevalent. This genotype is commonly detected in Turkey, Greece, Italy, and various African countries [6]. HBV is essential for HDV replication. Coinfection occurs when an individual is infected simultaneously with both viruses and superinfection when the HDV infection is acquired after HBV infection. These two clinical situations have different prognoses. The chronicity of coinfection is 2% to 7%, while the chronicity of superinfection is 70% to 90% [1,3,5,6].
The most important diagnostic method is to show IgM and IgG type Anti-HDV antibodies in serum samples. Anti-delta IgM occurs one month following acute infection and then anti-delta IgG is produced and continues for at least six months. In chronic situations high titers of total anti-HDV (mostly anti-delta IgG type) exist [7]. The decrease or loss of anti-delta IgM shows remission in chronic HDV infection. The diagnosis of chronic HDV infection is performed both by serological and virological assays. HDV-RNA is the first marker to become positive. Detection by polymerase chain reaction (PCR) indicates acute infection as well as ongoing infection. Loss of HDV-RNA is usually accompanied by a progressive decrease in anti-HD IgM titers [8]. The first choice in treatment is interferon, but response to treatment is 10% to 30% [9,10].

In this study we investigated anti-HDV seroprevalence and epidemiological features among HBsAg carriers attending the outpatient clinic at Izmir Tepecik Education and Research Hospital.

Methodology

In this study serum samples with HBsAg positivity were evaluated for anti-HDV by enzyme immunoassay (EIA) (Diaisorin, Saluggia, Italy) at Izmir Tepecik Education and Research Hospital’s Department of Infectious Diseases and Clinical Microbiology laboratory. Patients over the age of fourteen who were referred to our hospital were taken into the study. The samples were collected between 1 September 2007 and 30 August 2009. The alanine transaminase (ALT) values, hepatitis B (HBV), hepatitis C, HIV serological profiles, HBV DNA, alpha-fetoprotein (AFP), and histological activity scores of patients with liver biopsy were examined. HBV DNA was studied by real-time PCR method (Cobas Taqman, Roche, Sweden). Inactive carriers were defined as follows: HBsAg: positive; anti-HBs: negative; anti-HBe IgM: negative; anti-HBe Total: positive; HBeAg: negative/positive; anti-HBe: negative/positive; HBV DNA ≤ 2000 IU/ml and/or negative liver biopsy for chronic hepatitis. Chronic hepatitis B infection was defined as follows: HBsAg: positive; anti-HBs: negative; anti-HBc IgM: negative; anti-HBc total: positive; HBeAg: negative/positive; anti-HBe: positive/negative; HBV DNA ≥ 2000 IU/ml and/or chronic hepatitis proven by liver biopsy. The diagnosis of cirrhosis was performed by clinical and positive liver biopsy.

Results

A total of 3,094 HBsAg carriers were taken into the study. Seventy-nine (2.5%) of these patients had anti-HDV IgG positivity. The mean of age was 45.5 years (17 to 74 years); of these, 34 (43%) were female and 45 (57%) were male. Forty-two (53.2%) of these 79 patients were inactive hepatitis B carriers while 34 (43%) had chronic hepatitis B infection, two (2.5%) had liver cirrhosis, and one (1.2%) had hepatocellular carcinoma. Three patients (3.7%) had hepatitis C coinfection. Eight patients (10.1%) were HBeAg positive, antiHBe negative; 70 (88.6%) patients were HBeAg negative, anti-HBe positive; and one (1.2%) patient was both HBeAg and anti-HBe positive. The ALT mean value was 44.78 U/L and only 60.8% of the patients had normal ALT results (Table). Forty-six patients had alpha feto protein results and for ten (21.7%) of these patients the results were higher than normal. Eleven (13.9%) of the chronic hepatitis B patients underwent liver biopsy. These patients had a mean Knodell score and histological activity index of 12.7 and fibrosis score of 2.3 (Table). Forty-two (53.1%) of these 79 patients were inactive HBsAg carriers, while 34 (43.1%) of them had active chronic hepatitis B infection, two (2.5%) had liver cirrhosis and one (1.2%) of had hepatocellular cancer.

Table 1. Demographic features and the laboratory results of the patients

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean age</th>
<th>ALT (N:0-41IU/ml)</th>
<th>HBeAg</th>
<th>AFP (N:0-3.5 IU/ml)</th>
<th>Histological activity index/fibrosis score</th>
</tr>
</thead>
<tbody>
<tr>
<td>57% male</td>
<td>45.5 (17-74)</td>
<td>Normal</td>
<td>60.8%</td>
<td>Positive</td>
<td>11.4%</td>
</tr>
<tr>
<td>43% female</td>
<td></td>
<td>1-2 times</td>
<td>22.8%</td>
<td>Positive</td>
<td>11.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-5 times</td>
<td>12.6%</td>
<td>Negative</td>
<td>88.6%</td>
</tr>
</tbody>
</table>
Discussion

In this study we investigated anti-HDV seroprevalence and epidemiological features among HBsAg carriers admitted to outpatient clinics at Izmir Tepecik Education and Research Hospital. Seroprevalence of HDV in Italy, Eastern Europe, and Western Asia is higher than it is in the rest of the world and the infection is endemic in the Middle East [11]. Delta hepatitis prevalence is highest in some parts of Africa, South America, Romania, Russia and the Mediterranean region. Out of approximately 350 million carriers of HBV worldwide, 18 million people are infected with HDV [12,13]. Although the seroprevalence has decreased due to preventive measures and vaccination, it is still a problem.

Sakugawa et al. observed HBsAg positivity in 195 (9.6%) persons out of 2,028 healthy volunteers in Japan, and 46 of these individuals were positive for delta hepatitis (23.6%). The investigators also realized that the seroprevalence increased with advancing age [14]. In a study conducted in Russia, 265 HBsAg positive patients had 12.5% anti-HDV seroprevalence [15]. In Kyrgyzstan a series of 93 patients had 25.8% seropositivity [16].

According to a study held in Hungary, 118 chronic hepatitis B patients had 13.56% delta hepatitis seroprevalence [17]. In Italy HDV seropositivity among HBV carriers was 25% in 1983, and in 1992 this rate decreased to 14% and then decreased again to 8.3% in 1997 [18]. In northern India, a study on HDV seropositivity among HBsAg carriers showed 21.4% delta hepatitis seropositivity in chronic hepatitis B carriers and 10.7% in acute cases (a total of 206 cases of acute and chronic hepatitis B) and the mean rate was 14.2% [19]. Another study performed in India showed that out of 150 HBsAg positive patients (acute hepatitis B, chronic hepatitis B, fulminant hepatitis B, liver cirrhosis and hepatocellular carcinoma), nine (5.9%) also had HDV infection [20]. A recent study has shown a high HDV prevalence of 31.57% in HIV/HBV co-infected individuals in western Iran [21]. A study conducted in Wuhan City, China, revealed a low prevalence of HDV infection (2.22%) in intravenous drug users; however, the HBV and HCV prevalence rates were much higher in this population [22]. Jeong et al. showed that seven (3.6%) out of 194 HBsAg-positive patients were also positive for anti-HDV [23]. In another study that included 258 HBsAg positive patients from 10 health centers showed 1.2% HDV prevalence [24]. In a study held in Saudi Arabia, the HDV prevalence rate among HBsAg positive healthy donors was 3.3%, while the rate in clinic- and hospital-based HBsAg patients was 8.6% [25].

In different studies performed in our country, inactive HBV carriers had 0.9% to 16.2% HDV seroprevalence while, rates of 9% to 51.7% were seen in chronic hepatitis B patients, 2.5% to 21.8% in acute HBV patients, 23% to 74% in cirrhotic patients, and 6% to 33.3% in primary hepatocellular carcinoma patients [26,27]. The prevalence of delta hepatitis is less in Izmir compared to that in other parts of the country. The reason may be the lower seroprevalence of hepatitis B due to better socioeconomical conditions and the high rate of vaccination in this region.

Iskender et al. reported 2.33% anti-HDV seroprevalence in HBsAg positive patients [28], while Arıbas et al. observed seroprevalence rates of 1.2% in HBsAg positive patients [29]. In our study 79 out of 3,094 HBsAg positive patients (2.5%) had anti-HDV IgG seroprevalence. Of these 79 patients, 42 (53.1%) were inactive hepatitis B carriers, 34 (43%) had chronic hepatitis B, two (2.5%) had liver cirrhosis, and one (1.2%) had hepatocellular carcinoma. Our results are similar to those of other studies performed in Turkey.

Although HDV superinfection is less prevalent than coinfection, the prognosis is poor. The risk of having chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma is high. Pegylated interferon treatment is applied for a longer period but response to treatment is low. While rates are decreasing globally, transmission still occurs in some countries. New antivirals that are effective against HDV/HBV co-infection which is prevalent worldwide are needed. For these reasons, patients with hepatitis B infection should be further investigated for delta hepatitis infection.

References


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