Seroprevalence of hepatitis D virus in patients with hepatitis B virus-related liver diseases

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Received September 16, 2004

Background & objectives: Several reports indicated a declining trend in the occurrence of hepatitis D virus (HDV) infection in some geographical areas. However, no study has been conducted in India to evaluate whether a similar epidemiological change is occurring in this part of the world. The present study was undertaken to evaluate the seroprevalence of HDV in patients with hepatitis B virus (HBV) related liver diseases attending a Government hospital in New Delhi, and to assess any change in its epidemiology by comparing the results with seroprevalence figures reported in the past.

Methods: A total of 123 patients with HBV-related liver diseases comprising 32 cases of acute viral hepatitis (AVH), 5 of fulminant hepatic failure (FHF), 37 of chronic hepatitis (CH), 46 of cirrhosis and 3 of hepatocellular carcinoma (HCC). All patients were evaluated for the presence of delta antibodies using commercially available ELISA kits. Both IgM and IgG anti-delta assays were performed to differentiate between active and convalescent infection.

Results: The mean age of the patients was 35.6 ± 3.3 yr with a male : female ratio of 11:5. Of the 123 patients, serological evidence of delta virus infection was seen in 13 subjects (10.6%); 9 (7.3%) had evidence of past infection (IgG positive, IgM negative) and the remaining 4 (3.3%) recent infection (IgM anti-delta antibody positive). Evidence of HDV infection in acute viral hepatitis, fulminant hepatitis, chronic hepatitis, cirrhosis and hepatocellular carcinoma groups was found in 3.1, 20, 8.1, 15.2 and 33.3 patients, respectively.

Interpretation & conclusion: Our results suggest that delta infection may not be very common in Indian patients with HBV-related liver diseases. It is also possible that HDV epidemiology in this part of the world may be undergoing a transition towards decreasing prevalence.

Key words Acute viral hepatitis - chronic hepatitis - chronic liver disease - cirrhosis - fulminant hepatic failure - hepatitis B virus - hepatitis D virus - seroprevalence
Hepatitis D virus (HDV) is a defective RNA virus dependent on hepatitis B virus (HBV) infection for its replication and expression. HDV is well known to induce a spectrum of acute and chronic liver diseases. Acute infection with HDV can occur simultaneously with acute HBV infection or may be superimposed on chronic HBV infection.

Several reports indicated a declining trend in the occurrence of HDV infection in some geographical areas. For example, while HDV was responsible for a high proportion of cases of acute and chronic liver disease in Southern Europe during the 1970s, its seroprevalence was reported to have declined substantially in 1997. Huo et al from Taiwan have reported a decrease in HDV infection in hepatitis B surface antigen (HBsAg) carriers from 23.7 in 1983 to 4.2 per cent in 1995.

Though the presence of HDV infection in Indian patients with different types of liver diseases has been studied in the past, no study has been done to evaluate the change in HDV epidemiology in India. We undertook this study to evaluate the seroprevalence of HDV infection in patients with HBV-related liver diseases attending a government hospital in New Delhi and to evaluate any epidemiological change by comparing the results with seroprevalence figures reported in the past.

**Material & Methods**

A total of 326 consecutive patients with liver diseases attending Lok Nayak Hospital, New Delhi during February 2001 to February 2002 were included. These comprised 101 cases of acute viral hepatitis (AVH), 17 of fulminant hepatic failure (FHF), 97 of chronic hepatitis (CH), 103 of cirrhosis and 8 cases of hepatocellular carcinoma (HCC). All patients were screened for HBV infection, which was established by positivity for surface antigen HBsAg and/or core antibody IgM anti-HBc. This initial screening yielded the actual study group of 123 HBV-related liver disease patients consisting of 32 cases of AVH, 5 of FHF, 37 of CH, 46 of cirrhosis and 3 cases of HCC.

HDV detection was done by serology; both IgM and IgG anti-delta antibodies were detected to differentiate between active and convalescent infection. Approximately 8 ml blood was collected from each patient immediately after admission before any blood or blood products were transfused. Separation of serum was done within 3 to 4 h under complete aseptic conditions and stored at -70°C until use. The serological tests were performed using commercially available ELISA kits according to the instructions provided in the manufacturer’s manual. HBsAg was detected using Eliscan micro ELISA strips (Ranbaxy Diagnostics, England), IgM anti-HBc using anti-corse MB-96 (TMB) kit (General Biological, Taiwan), IgG anti-HBc by Melotest anti HBe kit (Melotec, S.A., Spain), HBeAg using Melotest HBeAg/Anti-HBe kit (Melotec, S.A., Spain) and IgM anti-HDV and IgG anti-HDV by ELISA kit, Diasorin, Italy.

**Results & Discussion**

The mean age of the patients was 35.6 ± 3.3 yr. There were 85 males and 38 females, the male : female ratio being 11:5.

Of the 123 patients, 13 were found to be reactive for anti-delta antibodies, yielding an overall HDV seroprevalence of 10.6 per cent. Of these, 9 (7.3% of total 123) cases had evidence of past infection (IgG anti-delta positive) and the remaining 4 patients (3.3% of total) had serological profile suggestive of recent infection (IgM anti-delta antibody positive) (Table). The overall exposure to HDV in acute liver disease patients was 3.1 per cent (1 of 32). In patients of chronic liver disease, delta seroprevalence was 12 per cent (10/83); 8 patients had serological profile suggestive of past/convalescent infection (IgG anti-delta positive) and the remaining 4 patients (3.3% of total) had serological profile suggestive of recent infection (IgM anti-delta antibody positive) and the remaining 2 subjects showed evidence of recent infection; both of the latter patients had HDV super-infection over HBV (IgM anti-HBc negative and IgG anti-HBc positive).

The anti-HDV positivity in AVH patients in our study was considerably low (3.1%), when compared with other Indian studies, where it has been reported to vary from 10.7 to as high as >30 per cent. In 1992, Amarapurkar et al from Mumbai had reported delta positivity in 16 per cent (23/148) of HBV-related AVH patients. In another study, Singh et al from Chandigarh could detect anti-delta antibodies in 10.7 per cent of their HBV-related AVH patients.
high HDV prevalence of 33 per cent (6/18) has been reported from Ludhiana by Ghuman et al; however, this study was carried out in paediatric population and had a small number of subjects.

Some countries have witnessed a declining trend in the prevalence of HDV infection. HDV had been found to be responsible for a high proportion of cases of HBV-related acute and chronic liver disorders in Southern Europe during the 1970s. However, by the 1990s, its seroprevalence had substantially declined. In Italy, the prevalence of anti-HDV among HBsAg carriers with liver diseases decreased from 25 per cent in 1983 to 14 per cent in 1992. A multi-center Italian study conducted in 1997 has reported HDV positivity of only 8.3 per cent in HBsAg-positive patients - a figure much lower than those observed in the previous two multi-center surveys performed in 1987 and 1992 (23 and 14%, respectively). The authors estimated that from 1987 to 1997, the rate of decrease in the proportion of HBsAg carriers with anti-HDV was about 1.5 per cent per year. A similar decrease (from 15.1% in 1983 to 7.1% in 1992) has also been reported from Spain. From Taiwan, Huo et al have reported a decrease in HDV endemicity from 23.7 per cent in 1983 to 4.2 per cent in 1995. The reduction in HDV seroprevalence has been postulated to result from a variety of factors such as active preventive measures directed against sexually transmitted diseases, promotion of disposable needles and better control of HBV infection itself. A similar epidemiological change may possibly be happening in India. However, several other factors that might contribute to the observed lower prevalence of HDV in the present study need further evaluation. For instance, composition and risk factor distribution within the respective study groups may account for the apparent inter-study differences. Additionally, epidemiological differences due ethnic or geographical factors, study methodology, etc., cannot be ruled out.

There appeared to be a large variation in the reported HDV seroprevalence in FHF (12.6 to 63%) from India, and the small number subjects evaluated in different studies (including the present study) limited the overall interpretation.

In chronic hepatitis and cirrhosis groups, anti-HDV antibodies were found in 8.1 and 15.2 per cent patients respectively, giving an overall positivity of 12 per cent in chronic liver disease. In contrast, higher seroprevalence of 21.4 and 19 per cent have been reported from Chandigarh and Mumbai, respectively.

A high frequency of dual HBV/HDV infection has been described in patients of HCC and it has been suggested that florid replication of both HBV and HDV and the resulting severe necro-inflammation may be an additional factor for promotion of HCC. No comparison could be made with earlier studies due to small number of subjects in the HCC subgroup in our study.

It has been suggested that HBV-HDV co-infections are significantly higher in acute hepatitis while super-infections predominate in chronic liver disease. This finding is reinforced by our study, wherein all anti-delta positive acute liver disease patients had HBV-HDV coinfection while all chronic liver disease patients with recent delta infection showed a serological profile typical of HDV super-infection over HBV. Thus, our results suggest that delta co-infection is more common in acute liver diseases while delta super-infection occurs more frequently in chronic liver disease.

In summary, HDV infection does not appear to be commonly prevalent in Indian patients with HBV-infected liver diseases.
related liver diseases in New Delhi. Our results also suggest that HDV epidemiology in this part of the world may possibly be undergoing a transition with a trend towards declining prevalence.

References


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