

ORIGINAL ARTICLE

PREVALENCE OF HEPATITIS D VIRUS (HDV) IN SOUTH GUJARAT

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ABSTRACT

Aim: Hepatitis D Virus (HDV) infects only patients that are already infected by hepatitis B virus (HBV). There is lack of data on the impact of Hepatitis D Virus (HDV) in patients with hepatitis B virus (HBV) in south Gujarat. This study was aimed at determining the seroprevalence of Hepatitis D Virus (HDV) in south Gujarat and does epidemiological studies on HDV among chronic Hepatitis B patients.

Methods: This study was carried out at tertiary hospital (New Civil Hospital, Surat). This study was done from March 2010 to April 2011. Total 141 consecutive HbsAg positive patients were included in this study.

Results: Out of 141 HbsAg positive patients 12 patients were positive for anti-HDV ELISA. High prevalence rate was found in middle aged man. HBV- HDV infection together cause more severe liver damage. HDV infection was more associated with blood transfusion.

Conclusion: The HDV infection is not uncommon. Coexistent infection with Hepatitis B aggravates the course of liver disease. One of the common route of HDV transmission is haematologic, suggesting the need for blood screening for HDV particularly in groups with numerous blood transfusions.

Keywords: Viral hepatitis, HbsAg, anti HD antibody, liver cirrhosis, hepatocellular carcinoma

INTRODUCTION

Hepatitis Delta virus (HDV) infection is present globally and infects human being already infected by Hepatitis B virus (HBV). HDV was first discovered by Rizzetto in the patients that were already infected by HBV in year 1980¹. Hepatitis delta virus (HDV) is a satellite RNA virus that depends on the envelope protein of the hepatitis B virus (HBV) to enter the hepatocytes and assemble new HDV particles. The particle size of HDV is about 36-nm that require hepatitis B surface antigen (HBsAg) for their enveloped and transmission². The HDV genome is a circular, negative sense, single-strand RNA, which is approximately 1700 nucleotides in length³.

Worldwide, more than 350 million people are considered to have chronic HBV infection. It has been estimated that approximately 5% of HBV carriers are co-infected with HDV⁴, leading to an estimated 15-20 million persons infected with HDV. The dual infection of HBV and HDV occurs in the form of co-infection or as a superinfection. The Super infection of HDV with HBV caused a progressive chronic liver disease up to (80%), which further enhances liver cirrhosis and hepatocellular carcinoma (HCC). Co-infection by both

HBV and HDV viruses causes more severe acute liver disease and is a higher risk for the development of fulminant hepatitis compared to only HBV infected patients⁵. Moreover, response to therapy is different and less satisfactory in patients with hepatitis delta virus (HDV) infection than hepatitis B virus (HBV) mono-infection.

Co-infections of hepatitis B with multiple hepatitis viruses are associated with diverse patterns of reciprocal inhibition of viral replication. Delta hepatitis occurs due to co-infection of HBsAg positive patients with hepatitis delta virus. There are inconsistent reports on the role of each virus in the pathogenicity of HBV/HDV infection. Some reports suggest that the activity of liver disease is mainly due to HDV while others implicate hepatitis B virus, regardless of the levels of HBV DNA, in the aggressive nature and progression of disease. In studies from Europe, HDV has frequently been shown to suppress HBV replication, and 70-90% of patients with hepatitis D are hepatitis B e antigen (HBeAg) negative, with low serum levels of HBV DNA. However, despite this influence of HDV on HBV, 15-30% of patients with hepatitis D are HBeAg and/or HBV DNA positive.⁶⁻¹²

Different rates of HDV infection among HBsAg-positive patients have been reported from worldwide. The infection was endemic in the 1970s throughout Southern Europe, and was responsible for a substantial proportion of cases of HBsAg- positive liver disorders^{13,14}. However, the prevalence of HDV had substantially declined in Italy from 23% in 1987 to 8.3% in 1997 as reported by Stroffolini et al¹⁵. A similar decline was noted in Taiwan, with prevalence decreasing from 23.7% in 1983 to 4.2% in 1996¹⁶, as well as in Spain and Turkey¹⁷. This decline in prevalence of HDV infection was achieved by enhancing awareness among the general public and by measures taken for vaccination against hepatitis B in these countries. Recently, a comprehensive report on the epidemiology of hepatitis delta in the Asia-Pacific region was published by Abbas et al¹⁸. According to this report, prevalence from different parts of Asia is variable, and ranges from 3-10% in India, 2-20% in Iran, 18% in Afghanistan and 3-8% in Saudi Arabia.

Eight phylogenetically distinct genotypes of HDV have been reported. Various genotypes are reported to be associated with different long term outcomes of infection¹⁹. Genotype 1 is the most frequent and found in Europe, Middle East, North America and North Africa; Genotype 2 is seen in the Far East; Genotype 3 was reported in the Amazonian region of South America; Genotype 4 was isolated in Taiwan and Japan; and Genotype 5 to 8 have been identified in Africans.

There is lack of data on the characteristics and impact of hepatitis delta virus on hepatitis B virus infection and its spectrum of diseases from South Asia. The aim of this study was to investigate the virological and clinical characteristics of patients infected with HBV/HDV infection.

METHODS

This study was carried out at tertiary hospital (New Civil Hospital, Surat). This was one year long study carried out between March 2010 to April 2011. A total of 141 consecutive HbsAg positive serum sample by enzyme linked immunosorbent assay (ELISA) were included in the study.

Demographics and physical findings were recorded in all patients. Serum samples of all patients were tested for biochemical parameters including complete blood count, total bilirubin, ALT, alkaline phosphatase, creatinine, and prothrombin time (PT) by standard laboratory methods. Serological test carried out were HbsAg and anti HD antibody by ELISA.

Statistical Analysis

All the data were analyzed and the summary statistic was carried out. Variables are given in the form of rates (%). The chi-square test was used for categorical variables. Values of less than 0.05 were considered significant.

RESULTS

Total 141 HbsAg positive patients were enrolled in the study. Out of the 141 patients, 12 were found to be reactive for anti-delta antibodies, yielding an overall HDV seroprevalence of 8.5%.

Table-1 Comparison of positive cases of anti HD antibody in different age

Age group(years)	M.V.Murhekar,SC Sehgal et al(20)	Present study
0-10	0	0
11-20	1	0
21-30	0	2
31-40	5	5
41-50	2	3
>50	0	2
Total	8	12

Table No: 1 shows the age wise distribution. From the table we observed positive cases of anti HD antibody are among the adult and old age. Higher prevalence rate for anti HD antibody observe in >30yrs.

Table 2: Distribution of anti-HD antibody according to sex, clinical groups and risk groups.

Characteristic	Cases Positive(%)
Sex	
Male	111 10 (9.0)
Female	30 02 (6.6)
Clinical groups	
Fulminant Hepatitis	53 08 (15.09)
Non-Fulminant Hepatitis	78 4 (5.12)
Jaundice without s/s of Hepatitis	10 00 (00)
Risk groups	
Blood Tranfusion	60 06 (10)
Surgery	30 01 (3.33)
Multiple Exposure	29 01 (4.16)
Other	22 04 (18.18)

Looking at the sexual preponderance, out of 141 enrolled patients, 78.7 % (n=111) were male and 21.2 % (n=30) were females. Among HDV positive patients 10 were males and 2 were females.

As shown in above table, prevalence rate amongst cases of fulminant hepatitis was as high as 15.09%, while in case of non-fulminant hepatitis, only 5.12 (%) cases were found positive for antibody and both the cases were of chronic active hepatitis. This difference is satisfactory significant as p value is 0.01, p<0.05. Fulminant hepatitis is more common in HDV infection.

Above table shows that rate of positive cases was higher in cases with past history of blood transfusion, which was 10% and in cases with history of multiple exposure and surgery, it was 4.16 and 3.33% respectively.

Table 3: Comparison study for prevalence rate in different risk groups.

Risk Group	Angeles castro et al		Velorie Kelly et al		Present study	
	Cases	+ve (%)	Cases	+ve (%)	Cases	+ve (%)
Blood Transfusion	15	02 (13.33)	24	00 (00)	60	06 (10)
Sexual	02	00 (00)	108	02 (1.85)	29	01 (4.16)
Others	158	32 (20.25)	274	18 (6.56)	107	05 (4.67)
Total	175	34 (19.42)	406	20 (4.92)	196	12 (6.12)

DISCUSSION

In this study mean age of HDV positive patients was 40+/-10. If we compare our study with the study of M.V.Murhekar, S.C.Sehgal et al²⁰, the cases of anti HD antibody positivity is more with adults and older age which correlates well with us. Another study done in Pakistan by Asad U Khan also has high prevalence in older (31.7%).

Table 4: Prevalence of Anti-D antibody in HbsAg positive

Study	HbsAg +ve	Anti-D +ve (%)
L.Matthyssen et al.	173	7 (4.04)
Gupta P,KarP et al	40	4 (10)
Al-Traifl,Ali A et al	780	67 (8.6)
M.V.Murhekar et al	223	8 (3.58)
Asad U khan et al	190	53 (28)
Present study	141	12 (8.5)

According to L.Matthyssen et al²¹, prevalence of anti-HD antibody was 4.04% amongst 173 cases of HBsAg reactive patients. Study conducted by Gupta Y et al²² among the HBV related cirrhosis of Liver shows that 10% were reactive for anti-delta antibodies. Our study can be well correlated with the study of Al-Traifl, Ali A et al²⁴ and Gupta P, et al. One study conducted in Pakistan by Asad U Khan et al.²⁵ shows very high prevalence (28%). We can infer that the prevalence rate varies widely as per geographic distribution. 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). A similar decrease (from 15.1% in 1983 to 7.1% in 1992) has also been reported from Spain and Taiwan. 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 happen in

India. 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., can not be ruled out.

Our studies suggest that HDV is more commonly associated with fulminant hepatitis. The study done by Gupta P, Kar Pet al²³ also shows that Hepatic Encephalopathy was seen in 75% of delta infected patients as compare to 13.88% of delta negative patients. There is a lot variation in the clinical course. More positivity of anti HD antibody in case having severe liver disease. There appeared to be a large variation in the reported HDV seroprevalence in Fulminant hepatic failure (12.6 to 63%) 6, 7, 10, 11 from India, and the small number subjects evaluated in different studies (including the present study) limited the overall interpretation. In non fulminant hepatitis anti-HDV antibodies were found in 5.12 per cent. 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 lack of subjects in the HCC subgroup in our study.

Above studies shows that variation in rate of positivity for anti HDV in different risk groups in different community. In Spain, HDV infection more common in blood transfusion which correlates with our study, while in London it was nil. In present study, there was no case of drug addiction. The Group others include the cases with non specific history.

There is difference in life style as well as risk factor in different area, so one must know the prevalence incidence in their region.

CONCLUSION

The prevalence rate of Hepatitis D virus infection was 8.5% amongst HbsAg positive patients at tertiary hospital of South Gujarat. Prevalence of HDV infection was more common in middle aged male. Blood tranfusion is the commenest mode of transmission. The HDV infection is not uncomman. Coexistent infection with Hepatitis B aggravates the course of liver disease. One of the common route of HDV transmission is haematologic, suggesting the need

for blood screening for HDV particularly in groups with numerous blood transfusions. Clinician dealing with the Liver Disease should be made aware of the danger of twin infection with HBV and HDV.

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