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High Rates of Hepatitis Delta Virus Superinfection / Coinfection in Balochistan

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ABSTRACT

Hepatitis B carrier rate is still very high in Pakistan, especially in Balochistan, where in some areas almost 16% of the population is positive for HBsAg. Delta virus, also known as hepatitis D virus, only affects those suffering from Hep B infection (HbsAg positive). A study was carried out to check for Hepatitis Delta virus infection in these patients. This study showed that 35% HbsAg reactive patients had either coinfection or superinfection with the Hepatitis delta virus. These rates are much higher than the other studies, and are alarming. Vaccination against Hepatitis B virus can also prevent this infection. Awareness and prevention at community level is required.

Key words: Hepatitis, delta virus, anti HDV, Hepatitis B.

INTRODUCTION

Chronic hepatitis B is a common disease with an estimated global prevalence of approximately 5% of the world's population[1]. There are wide ranges in the prevalence of HBV infection in different parts of the world. In Southeast Asia, China, Philippines, Indonesia, Middle East and Africa the prevalence is high, with HBsAg positivity rates ranging from 8% to 15%.[2] Chronic Hepatitis B infection rate is still very high in Pakistan even after availability of vaccination, especially in Balochistan, where is some areas almost 16% of the population is having HbsAg reactive in their serums[6].

Hepatitis delta virus (HDV) is a unique RNA virus that requires a helper function provided by hepatitis B virus (HBV) for replication[1,2,3]. Thus, it only affects those suffering from Hepatitis B infection (HbsAg positive). HDAg can elicit a specific immune response in the infected host, consisting of antibodies of the IgM and IgG class (anti-HDV). In the HDV infected individuals, the timing of appearance and the level of HDV RNA, HDAg and anti-HDV in the serum allow the three HDV-related clinical entities to be discriminated:

- Acute HBV/HDV coinfection
- Acute HDV superinfection of a chronic HBV carrier
- Chronic HDV infection

Incidence and Prevalence

There are 15 million persons infected with HDV worldwide. Areas of high prevalence include Italy, certain parts of Eastern Europe, the Amazon basin, Colombia, Venezuela, Western Asia, and some Pacific Islands. In the United States, an estimated 7500 HDV infections occur annually.[3] The prevalence of HDV infection in patients with HBV infection is low in the general population, as represented by blood donors, and highest among persons with percutaneous exposures, such as injection drug users (20%–53%) and hemophiliacs (48%–80%).[3] Although HBV is required for replication of HDV, the geographic distribution of HDV does not match that of HBV precisely, suggesting that other factors, such as age of infection, may determine the prevalence of HDV within a population of HBV-infected persons.

In Pakistan, studies show much higher rate of infection ranging from 26-36%. [6, 8]

Transmission

The modes of transmission of HDV are

similar to those of HBV infection, and percutaneous exposures are the most efficient. In a study of 88 HBV-infected drug users in New York, HDV and HIV infections were present in 67% and 58%, respectively.[4] Some HDV-infected HBV carriers appear to have a more benign clinical course. Hemophiliacs and other persons who receive large amounts of pooled blood products are at increased risk of acquiring HDV infection.[5]

Both hepatitis B and hepatitis D are preventable diseases. A timely and effective vaccination against hepatitis B virus can decrease the risk of, not only hepatitis B, but also Hepatitis D infection.

Aims and Objectives:

A study was carried out to check for status of Hepatitis Delta virus coinfection / superinfection in the patients, who were having HBsAg reactive in their serum. Anti HDV IgG antibody was the only available test, which can indicates a previous infection that could either be coinfection or superinfection with hep B.

The primary objective of the study was to determine the Hepatitis Delta infection in HBsAg positive patients. Secondarily, it was tried to look for hep D association with ALT levels, HBV DNA and HBeAg status. Also to identify the risk factors in these patients.

Inclusion Criteria:

- All patients positive for HBsAg by ELISA
- Both sexes

Exclusion Criteria:

Patients having auto-immune disorders, alcohol abuse and chronic hepatitis C were excluded

MATERIAL AND METHODS

A total 60 patients, in whom HbsAg by Elisa was found to be reactive, were included in the study. A detailed history, including pervious history of jaundice, any operation or injection therapy, blood transfusion, dental treatment, sexual exposure and IV drugs abuse was obtained. After a thorough physical examination, laboratory and radiological investigations including liver function tests, complete blood count, abdominal ultrasound, Hep B Virus DNA by PCR (qualitative), HBeAg, AntiHBe antibody and anti HDV IgG antibodies were done.

Patients were stratified in various groups according to their area of residence

Statistical Analysis

Statistical analysis was performed on SPSS version 13. Frequency of hep D antibody in HbsAg postive patient was checked. Chi-square test used to analyze the association between anti HDV IgG and HBV DNA (Qualitative), HbeAg, AntiHBe anti body, serum ALT levels and abdominal ultrasound. The relationship with the risk factors, like tattoo, blood transfusion, operation and dental treatment was also analyzed. A p-value of <0.05 was selected as significant.

RESULTS

A total of sixty patients with HBsAg reactive were included. Forty eight were male and twelve were females. The mean age was 31±9.72 years. History of dental treatment was given by 6 patients, while history of blood transfusion in only one patient. Tattoos were found in two patients (Table 1).

Table 1: Frequency of risk factors

Risk factors	No.	Percent	P-value
H/O Dental treatment	6	10	>0.05
H/O blood transfusion	1	1.6	>0.05
H/O operation/injection	9	15	>0.05
Tattoos	2	3.2	>0.05
H/O IV drug abuse	00	00	>0.05
H/O unsafe sexual exposure	00	00	>0.05

Out of these 60 patients, having HbsAg positive, the Anti HDV IgG anti body was positive in 21 (35%) negative in 37 (63%), border line in 1 patient, while one report was missing (Table 2).

Qualitative analysis of HBV DNA by PCR was performed in 58 patients. None of our patients, having anti HDV IgG antibodies reactive, was positive for HBV DNA by PCR (qualitative) in his serum. HbeAg was reactive in only 2 patients while it was negative in 18 patients with anti HDV IgG

antibodies, and data was missing for one patient. AntiHBe antibody test was positive in 18, while it was negative in three patients (Table 3).

Table 2: Percentage of Anti-HDV IgG reactivity.

Anti-HDV IgG	Number	Percent
Reactive	21	35.0
Non-reactive	37	61.7
Borderline	1	1.7
Total	59	98.3
Missing	1	1.7
Total	60	100.0

Table 3: Comparison of anti-HDV IgG with HBV DNA and HBeAg.

	Anti HDV Reactive	Anti HDV Non-Reactive	p-value
HBV DNA (qualitative) detected	00	58	>0.05
HBeAg Reactive	02	18	>0.05
AntiHBe antibody Reactive	17	28	>0.05
Normal ALT	09	23	>0.05
ALT >2xULN	3	12	>0.05
ALT >2xULN	9	1	>0.05

In patients who tested positive for Anti HDV IgG, serum ALT level was twice the upper limit of normal (2xULN) in three patients (14%), more than 2xULN in nine patients (43%), while it was (normal) less than 1xULN in 09 patients (43%).

Abdominal ultrasonography was normal in 12 (57%) patients and findings of chronic liver disease were observed in 9 (43%) patients having antiHDV IgG reactive.

DISCUSSION

Hepatitis delta virus infection is a slowly progressive deadly disease, in which the patients ultimately end up with liver cirrhosis and its complications.

In this study, it was observed that most of the patients had HBV DNA and HBeAg negative and antiHBe antibody reactive. These three findings reflect a low HBV infection, but as these patients had hepatitis delta virus superinfection, the progression to the chronic hepatitis was augmented. Serum aminotranferase (ALT) levels were also above normal in 57% of patients, and ultrasonography showed liver parenchymal changes in 43% of patients. Both these parameters indicate progressive liver damage, which will ultimately result in liver cirrhosis.

Although the study was done in a small number of patients, but it shows that about 35% of Hepatitis B patients have either coinfection or superinfection of hepatitis delta. The various studies indicate a range of 23-36% delta infection [6, 7, 8]. Our study also shows much higher rate of infectivity. The primary reason for this is unawareness, both at the level of treating physicians and the patients. Others are reuse of syringes, lack of proper sterilization of instruments and unavailability of hepatitis B vaccination.

CONCLUSION

Much higher rate of infectivity is seen in this study, which is worrisome. Hepatitis delta virus is a preventable disease since it only affects those having Hepatitis B virus infection. Thus, vaccination against Hepatitis B on a community level can actually help in the prevention of both Hepatitis B and delta virus infection.

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