Frequency of Hepatitis D Virus in HbsAg Positive Patients Presenting to Liver Clinics

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Abstract

Background: In Pakistan, viral hepatitis endures as a distressing health issue. This study was conducted to determine the presence of hepatitis D virus infection in HBsAg positive patients and to assess its relationship with gender, age and serological variables in Pakistani population.

Methods: A cross sectional study was carried out at liver clinic of Holy Family hospital from April 2011-April 2016. 153 HBsAg positive patients were included. Serological tests for HBeAg, HBeAb and Anti-HDV by ELISA and HBV DNA by PCR technique were performed while Patients with acute HBV infection or other co-morbidities were excluded.

Results: Out of total 153 patients, 25 (16.6%) were positive for Anti-HDV amongst whom 16(64.0%) were males and 9 (36.0%) were females (p= 0.97). 13 (52.0%) were upto 30 years of age and 12 (48.0%) were above 30years of age (p=0.36). Amongst the Anti-HDV positive patients, 14(60.9%) were negative for HBeAg (p=0.004) whereas HBV DNA was positive in 66.2% of HBeAg negative patients (pre-core mutants)(p=0.00). However, no significant relation of Anti-HDV with HBeAb and HBV DNA was ascertained.

Conclusion: There is a considerable prevalence of HDV in HBsAg positive patients.

Key words: Hepatitis delta, Hepatitis B, Viral hepatitis, HBsAg, Co-infection, HDV superinfection, HbeAg, Prevalence,Pakistan.

Introduction

Hepatitis delta virus (HDV), the reason for most extreme type of viral hepatitis, is a satellite RNA virus that relies upon the envelope protein of the hepatitis B virus (HBV) for its replication and expression.1 Up to 5% of the world's population is infected with hepatitis B infection, and likely 5% of the HBV chronic carriers have hepatitis D virus (HDV) co-infection and super-infection, in this manner an expected 15-20 million of world's population is contaminated with HDV2,3 with roughly 1 million fatalities occurring annually.4 Its prevalence is high in Italy, Eastern Europe and western locale of Asia and seems, by all accounts, to be endemic in the Central East.5 In Pakistan, viral hepatitis endures as a distressing health issue. Mumtaz et al6 stated that HDV infection is present in 16.6% of hepatitis B infected patients in Pakistan, with high prevalence (58.6%)7 being accounted for in Southern Pakistan.8

Hepatitis D infection (HDV) disease affects all age groups around the world. However, it doesn't have uniform distribution and its general pattern is parallel to that of hepatitis B infection (HBV).9 There is higher seroprevalence of HDV in younger male subjects who are HBsAg positive.10 Delta contamination is correlated with negative HBeAg status and decrease in HBV replication.11 It is noted that HDV has a tendency to aggravate the course of HBV-related liver infection. The prevalence of HDV related fulminant hepatitis is 10 times higher than that seen for other viral hepatitis.12 Considering the facts mentioned above, this study is designed to enable us to determine the magnitude of hepatitis D virus in HBsAg positive patients in Pakistan. Our study is unique of its kind as no such previous study has been conducted in this area. Furthermore, it will also emphasize the health providers and policy makers to implement effective preventive programs, as designed by other countries, to reduce its prevalence rate.

The objective of our study was to determine the frequency HBsAg positive patients with positive hepatitis D virus infection, visiting liver centre of Holy Family Hospital and also to assess any existing relationship of HDV infection with gender, age and serological variables.

Materials and Methods

This cross sectional descriptive study was conducted at the Liver centre of Holy Family Hospital from April 2011–April 2016. The study was approved by the Institutional Research Forum of Rawalpindi Medical College and Allied Hospitals Study population comprised of HBsAg positive patients from 16-65 years of ages. All HBsAg positive patients were included while those with other medical and surgical co-morbidities were excluded.

Using WHO sample size calculator, keeping confidence level 95%, anticipated population

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proportion 0.166, and absolute precision 6%, the minimally required sample size was calculated to be 148. But we included 153 patients. Systematic random sampling technique was used for this study.

The laboratory tests comprised of HBV serum markers, HBeAg, HBeAb and Anti-HDV by ELISA and HBV DNA by PCR technique. HBeAg positive were the patients tested positive for Hepatitis B envelop antigen by ELISA and HBV positive were the patients with HBV DNA level above 50 IU/ml. To determine association between age group with hepatitis D prevalence, Chi-square test at 5% level of significance was applied while for cross tabulations with more than 10% of cells having expected count less than 5, Fischer’s exact test at 5% level of significance was applied. p-value less than 0.05 was considered statistically significant.

**Results**

A total of 153 patients comprised of 110 (71.9%) males and 43 (28.1%) female patients. The mean age of all 153 patients was 32.27 ±12.73 years while the youngest patients was 16 years old and eldest was 65 years old. 79 (51.6%) patients were up to age of 30 years while 74 (48.4%) were above 30 years of age amongst all study participants. Twenty five (16.6%) were tested positive for Anti-HDV, amongst whom majority (71.5%) were males (p-value=0.36 indicating an insignificant association of anti-HDV with gender). Thirteen (52.0%) patients amongst these 25 were up to 30 years of age and 12 (48.0%) were above 30 years of age. When association of Anti-HDV positivity with age group was assessed, a p-value of 0.97 showed that statistically significant association did not exist. The socio-demographic and serological distribution of patients with Anti-HDV positivity or negativity (Figure 1).

![Figure 1. Socio-Demographic And Serological Distribution According To Anti HDV Status.](image1)

![Figure 2. Association between Anti HDV and HbeAg serology.](image2)

![Figure 3. Hbe Ag Serology of HBV-DNA positive patients.](image3)

Discussion

Hepatitis B virus (HBV) infection is a universally widespread disease which carries a high incidence of mortality and morbidity. The prevalence of HBV/HDV co-infection in our region was 16.6% which is less than that delineated by Seetlani et al in Southern part of Pakistan showing an extensive spread of 58.6%.

Nevertheless, additional studies conducted in Karachi and Larkana showed the prevalence rate of 28.1% and 26.8% respectively. HDV is highly...
indigenous with wide range of prevalence between 2 -17.3% in Iran, 5-10% in India and 24.4% in Bangladesh. This increased prevalence can be attributed to the use of unsterilized syringes and surgical instruments, reuse of blades by barbers and transmission by sexual contact. In middle eastern countries, the prevalence of Anti-HDV serological markers was noted as 2%, 3.3%, 5.2%, and 31% in Jordan, Saudi Arabia, Turkey, and Kuwait respectively. However, a seroprevalence of less than 5% was documented among distinct areas of Europe due to HBV vaccination, growing awareness, improved protective measures and better financial conditions.

In this study, the seroprevalence of Anti-HDV was found more in young males (64%) with age up to 30 years (52%), which is consistent with earlier reports from Italy and Pakistan where maximum prevalence was found in 18-26 years old male as reported by Pesquini et al and Abbasi et al. One probable justification could be the higher rate of intravenous drug abuse, therapeutic injections and vertical transmission in this group of patients.

In our study we also found that 60.9% Anti-HDV positive patients were negative for HBeAg, which shows a statistically significant association between HDV seroprevalence and HBeAg (p=0.004). In a study conducted by Behrooz et al, HDV positive patients displaying negative result for HBeAg was more than 80%. Various other studies reported analogous findings with up to 90% of HDV positive patients showing negative HBeAg status. This can perhaps be a result of suppression of Hepatitis B virus by HBV/HDV co-infection.

Our data also showed 66.2% of HBeAg negative patients who came out to be positive for HBV DNA(pre-core mutants), implying another statistically significant association (p=0.000) which goes in coherence with another study conducted at Tunisia where this relationship came out to be 90%.

Conclusion
Our study showed a considerable prevalence of HDV in HbsAg positive patients.

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References