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HEPATITIS DELTA;

PREVALENCE OF HEPATITIS DELTA IN PATIENTS WITH CHRONIC HEPATITIS B INFECTION

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ABSTRACT… Objectives: The objective of this study is to prevalence of hepatitis delta in patients with chronic hepatitis B infection. **Study Design:** Cross-sectional study. **Period**: One year starting from February 2016 to January 2017. **Setting:** Patients OPD and admitted to Dow university hospital and Zubaida Medical Center Karachi. **Methods:** Hepatitis B surface antigen (HbsAg) were analyzed for the presence or absence of Hepatitis D antibody (Anti HDV). 368 patients with chronic hepatitis B were included to be part of this study. Patient's age, duration of illness and previous treatments were recorded. HBV and HDV virus presence was confirmed by using Polymerase chain reaction (PCR). **Results:** Out of 368 patients with chronic HBV infection, 291 (79.07%) were males and 77 (20.92%) were females. The male to female ratio was 3.7:1. Patients were aged between 35-60 years. 251 (68.2%) were positive for anti HDV. 211 of them were males (84%) and 40 were females (15.9%). **Conclusion:** We have concluded that HDV infection is associated with higher incidence of hepatocellular carcinoma in patients. Effective and early treatment of HDV can reduce the frequency of patients advancing to decompensated chronic liver disease and hepatocellular carcinoma.

Key words: Hepatitis Delta Virus, Chronic Hepatitis B Infection, Hepatocellular Carcinoma.

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INTRODUCTION

Globally millions of individuals are infected concomitantly with hepatitis B virus (HBV) and hepatitis D virus (HDV). It has been estimated that annually nearly 2 billion people are exposed to HBV, 350 million individuals are infected with HBV around the globe whereas 12-20 million are co-infected with HDV.[1] Around 0.1-0.2% individuals in the United States and Western Europe are infected with HBV. This percentage is 2-8% in the Mediterranean countries and Japan whereas in Southeast Asia and sub-saharan regions the number rises to 8-20%.[2,3] In Pakistan the prevalence is estimated to be in between 16-57% in general population with majority being young males living in rural areas[4,5]

HBV is DNA virus with high genetic variability and eight genotypes A-H. Genotype I and J are recently introduced and show geographic distribution. These genotypes differ within 8% of the entire genome from one another. These structural and functional differences may account for different clinical presentation, treatment response and failure and interactions with vaccines. HDV is a defective RNA virus which requires the presence of HBV for its replication. HDV also has eight different genotypes.[6-8] Each genotype has its own distribution pattern as well as clinical presentation and course. The common routes for transmission of HBV include transfusion of unscreened blood, unprotected sex, sharing and recycling needles in hospitals or among IV drug abusers, needle prick injuries, renal dialysis and also long term non-sexual contact with HBsAg positive individuals[11], however in areas of high prevalence, vertical and horizontal transmission of HBV has also been reported.[9,10]

Infection with HDV can either result from co-infection or super infection. Co-infection has been seen to result in clearance of HBV-HDV in 95% patients whereas super-infection is associated with HDV chronicity in around 90% cases.[13] In terms

of severity of hepatic damage and progression of disease, chronic HDV infection is more severe than chronic HBV monoinfection, with a rapid progression to decompensated liver disease as well Hepatocellular carcinoma.[1] Available treatment options for HDV infection include PEG-INF or conventional INF only. In the absence of contraindication to INF therapy, PEG-INF can be given but the sustained virological response rate is only about 25%. in decompensated liver disease secondary to HDV co infection, liver transplant remains the only treatment option). Worldwide with the advent of new and improved vaccination protocols against HBV in the last few decades, the frequency of HBV infection and HDV has reduced dramatically among the developed western countries but in Southeast Asia, where the healthcare facilities are still not efficient, the prevalence of HBV and co infection with HDV is largely undetermined. The purpose of this study is to find the frequency of HDV infection in chronic HBV patients, so HDV antibody screening may be recommended early or soon after the diagnosis of HBV infection and patient may be benefitted with the therapeutic option of PEG-INF.

METHODS

This is a cross-sectional study done over the period of one year starting from February 2016 to January 2017. Patients OPD and admitted to Dow university hospital and Zubaida Medical Center Karachi with Hepatitis B surface antigen (HbsAg) were analyzed for the presence or absence of Hepatitis D antibody (Anti HDV). 368 patients with chronic hepatitis B were included to be part of this study. Patient's age, duration of illness and previous treatments were recorded. HBV and HDV virus presence was confirmed by using Polymerase chain reaction (PCR). Other investigations included CBC, serum albumin, SGPT, serum bilirubin and ultrasound abdomen. Data was analyzed using SPSS v.20.

RESULTS

Out of 368 patients with chronic HBV infection, 291 (79.07%) were males and 77 (20.92%) were females. The male to female ratio was 3.7:1. Patients were aged between 35-60 years. 251 (68.2%) were positive for anti HDV. 211 of them were males (84%) and 40 were females (15.9%).

Variable	No. Patients	Percentage
Gender		
Male	291	79.07%
Female	77	20.92%
Age		
25 to 35 years	127	34.51%
36 to 45 years	128	34.78%
46 to 55 years	69	18.75%
56 to 65 years	44	11.95%
Marital status		
Single	79	21.49%
Married	289	78.53%
Living status		
Rural Area	101	27.44%
Urban Area	192	52.17%
Abroad	75	20.38%
Anti-HDV positive		
Positive	251	68.20%

Table-I. Demographic variables n=368

Variable	No. Patients	Percentage
Gender		
• Male	211	84.0%
• Female	40	15.9 %

Table-II. HBV-HDV co-infection:

DISCUSSION

The highest rates of hepatitis B virus in the world are found in western amazon basin including areas of Brazil, Peru, Ecuador, Venezuela and Colombia.[6,14] The incidence of HBV is increasing dramatically in northern and central Europe because of infected individuals emigrating from endemic regions as well as increased rate of IV drug abuse.[15] Co-infection with HDV is common in Africa and Middle east however in USA co-infection with HDV is restricted to individuals with IV drug abuse or others at high risk.[1,16] Sagnelli et al reports that HBV genotype D was the most common genotype infecting residents of Italy since decades and was responsible for 95% cases of acute and chronic hepatitis B cases but now this percentage has fallen down to 40% due to migrants moving from different areas to Italy.[17,18]

Crispim et al. reports his study result, which was conducted in the Western Amazon region. 70.5% of individuals from his study were mono-infected

with HBV only. The most common genotype in mono-infected patients was genotype A followed by genotype D and F. Others followed co-infection with HDV. Only HDV genotype 3 was found. HBV-HDV co-infection rate was 65% in outpatient subjects, 47% in individuals from Eirunepe (from southwest part of Amazon) and 8.5% in blood donors. The most common genotype associated with co-infection was HBV/F-HDV/3 followed by HBV/A-HDV/3 and HBV/D-HDV/3. Patients infected with HBV genotypes A and B have better response on treatment with interferon than patients infected with genotype C and D.[15]

Asad et al reports his study results which are similar to our study. He reports 28% prevalence of HDV infection whereas our study reports 21% prevalence. His study reports higher incidence of HDV-HBV infection in males as compared to females. 31% males were infected whereas 23% females were infected. Our study shows 84% males whereas 16% females. Both of these studies are conducted in Pakistan. The difference between Asad et al's study and our study is that Asad's study includes data collected from various regions of Pakistan whereas our study reports results from patients admitted in our hospital with chronic HBV over the study duration. Dow University Hospital is a semi-private hospital which receives patients from various parts of Pakistan but majority of individuals belong to areas from sindh. Our study includes 101 patients from rural areas whereas 192 patients from urban areas and 92 patients from regions outside Pakistan. Asad et al also reports the prevalence of HBV-HDV infection to be 67% in Sindh, 6% in Khyber Pukhtunkhwa (KPK) and 4% in Punjab.[19] Two other studies conducted in Pakistan, reports the prevalence of HBV and HDV infection to be 16% and 57% however the results of these studies were based on ELISA whereas Asad et al's study and our study report our study results on basis of PCR analysis. PCR is more specific for the diagnosis of infection than ELISA.[4,5] In 2005, a survey was conducted among 8721 HBV patients. Only patients aged above 14 years were included. This survey reports the prevalence of HDV infection to be 16.6%.[20] Seetlani et al, reports 46.2% prevalence of HDV infection in 2009. His study was conducted among 362 patients form Karachi and patients presenting to clinic in Jacobabad. He reported that majority of patients belonged to areas of sindh and balochistan.[21]

Treatment options for patients co-infected with hepatitis B virus and hepatitis D virus include oral nucleosides for duration of at least one year. If treatment with oral nucleosides and nucleotides is not effective, interferon therapy can be offered. The response rate for treatment of co-infection with interferon therapy has been reported to be 15% whereas that for super-infection has been reported to be 5%. However it is observed that these results are short-lived and reoccurrence of infection has been reported.[22,23]

HDV is also common with HIV infection. HBV and HIV are similar in intravenous drug use being one of the common routes of acquiring both of these infections. HDV can also be acquired by this route. Therefore it is not uncommon to have HBV-HDV and HIV co-infection.[24,25]

CONCLUSION

Our study reports HBV HDV infection to be 68%, HDV infection is associated with higher incidence of hepatocellular carcinoma in patients. Effective and early treatment of HDV can reduce the frequency of patients advancing to decompensated chronic liver disease and hepatocellular carcinoma.

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To climb steep hills requires
a slow pace at first.

– William Shakespeare –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Hafeezullah Shaikh	Conception and design, Critical revision of the article for important intellectual content.	
2	Ahsan Mobin	Statistical expertise, Critical revision of the article for important intellectual content.	
3	Imtiaz Manzoor	Drafting of the article	
4	M. Ashraf Ebrahim	Drafting of the article	