Prevelance of Hepatitis B & D Coinfection in Acute Active Viral Hepatitis in A Tertiary Care Hospital

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ABSTRACT

Introduction: In patients suffering from hepatitis B virus (HBV), Hepatitis delta virus (HDV) infection is a cause of coinfection and superinfection. The global prevalence of HDV depends largely on the geographical location. There is sparse data on prevalence of HDV and its co infection in HBV patients in India. This study was aimed to determine the prevalence of HDV in HBV-infected groups, utilizing serological methods.

Material and methods: This was a prospective cross-sectional study conducted from January 2016 to June 2016. Serum samples of 257patients that had tested positive for HBV (HBsAg) with or without co-positivity for other hepatitis viruses (HCV, HAV and HEV) were included in the study All the specimens were tested for anti-HDV immunoglobulin (Ig) M (IgM) and IgM-HBcAg and HBeAg to ascertain acute sinfection status

Results: HDV infection was observed in only one patient out of 89 samples tested making an overall prevalence of 1.1%.

Conclusion: The present study provides evidence that HDV infection is very low(1.1 in this part of India. However further prospective studies with larger sample size are warranted.

Keywords: Hepatitis B Virus, Hepatitis Delta Virus, Prevalence

INTRODUCTION

In 1977 Mario Rizzetto and colleagues described a novel antigen in the nucleus of hepatocytes derived from patients infected with Hepatitis B virus., which is a defective RNA virus belonging to the family Deltaviridae and genus *Deltavirus*. It utilizes the envelope of hepatitis B virus (HBV), i.e. hepatitis B surface antigen (HBsAg), for the transmission of infection.[1,2] Because HDV particle assembly and release are dependent on the obligatory presence of HBV within the same hepatocytes; a productive HDV infection is invariably associated with HBV infection.HDV infection leads to more severe liver disease than HBV monoinfection with accelerated fibrosis progression, earlier hepatic decompensation and an increased risk for the development of hepatocellular carcinoma.[3] The researchers have shown that very little inoculums are sufficient for transmission. These routes include blood transfusion, intravenous drug abuse, sexual contact and nosocomial infection. There are some evidences that infection could be transmitted between family members.[4,5,6]

Co-infection and Super infection

The hepatitis D virus requires the presence of an HBV infection or at least carrier state. Therefore HBV is referred to as the helper virus. There are two important terms to describe its dependence on HBV. Co-infection is when HDV infects a person at the same time as HBV. Superinfection is when HDV infects a person who is a chronic carrier of HBV.[2] Globally, HDV infection is found in more than 15 million people. Its prevalence is mostly focused in Italy, Eastern Europe, and western Asia.[7] Recently, a study reported that there are about 350 million carriers of HBV infection worldwide of which 18 million are infected with HDV . Countries such as Iran and Pakistan showed an increase in HDV prevalence. On the other hand, countries like Turkey, India, Australia, China, Japan, and Taiwan, which had a very high HDV prevalence in the past, have shown a decline in the incidence rate, although a high prevalence rate persists in some of them.[8]

Study objectives were to study the prevalence of dual/ co infection of Hepatitis B and Hepatitis D virus in acute hepatitis B infected patients and to determine the HBeAg of these dually infected patients and establish a relationship if existed between the expression of hepatitis B e antigen and HDV infection.

MATERIAL AND METHODS

Serum samples of 257patients that had tested positive for HBV (HBsAg) with or without co-positivity for other hepatitis viruses (HCV, HAV and HEV) were included in the study. These samples were taken from 5000 samples received from January 2016 to June 2016 in the virology division of Sheri-Kashmir Institute of Medical Sciences, Srinagar from patients presenting with symptoms of acute hepatitis. Samples were screened for different hepatitis infections, viz. HAV, HBV, HCV and HEV, as per the suggestive clinical suspicion. Samples that had tested positive only for HAV, HEV or HCV were excluded from the study

To ascertain that the samples (257 HBsAg positives) are qualifying the criteria of acute status of hepatitis these were further analysed for IgM-HBcAg and HBeAg to determine the viral activity. Out of these positive samples 89 were

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How to cite this article: Nisar Q, Lone MS, Shafi A, Ahmad J. Prevelance of hepatitis B & D coinfection in acute active viral hepatitis in a tertiary care hospital. International Journal of Contemporary Medical Research 2021;8(2):B12-B14.

DOI: http://dx.doi.org/10.21276/ijcmr.2021.8.2.12

included in the study and tested for the presence of Anti HDV IgM antibodies to determine the co- / dual infections of HBV and HDV so as to establisha relationship existing between the acute / active viral hepatitis and HDV infection, if any.

RESULTS

A total of 5000 blood samples were screened for HBsAg .Out of 5000 samples, 257(5.14%) were HBsAg positive. Out of 257 HBsAg positive samples 89 samples were having IgM-HBc levels more than 5mIU/ml rendering them positive for HBcAg-IgM which was suggestive of acute hepatitis B infection. Furthermore out of these 89 HBsAgand HBcAg-IgM positive samples 36 samples tested positive for HBsAg Most of the patients i.e. 30 (33.7%) which were positive for HBsAg belong to the age group of 32-42 years followed by 21(23.6%) belong to age group of 21-31 years followed by the least number of patients in <20 years of age group i.e. 2 (2.2%) patients (fig-1).

Out of 58 male patients maximum number of patients i.e. 19 (32.8%) belong to the age group of 43-53 years followed by 17 (29.3%) patients belong to age group of 32-42 years and the least number of patients i.e. 01 (1.7%) in age group <20 years of age. Out of 31 Female patients maximum number of patients i.e. 13 (41.9%) belong to the age group of 30-37 years followed by 09 (29.0%) patients belong to age group of 38-46 years and the least number of patients i.e. 01 (3.2%) in age group <20 years of age.

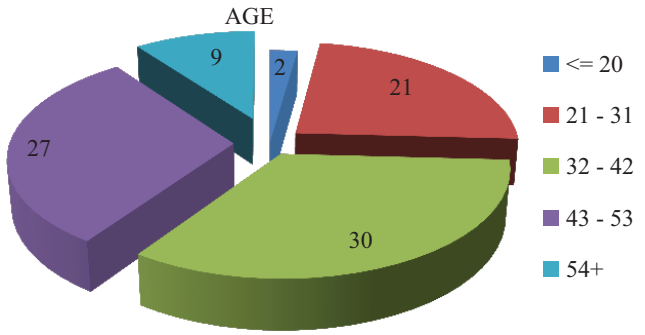

Figure-1: Age wise distribution of patients in general.

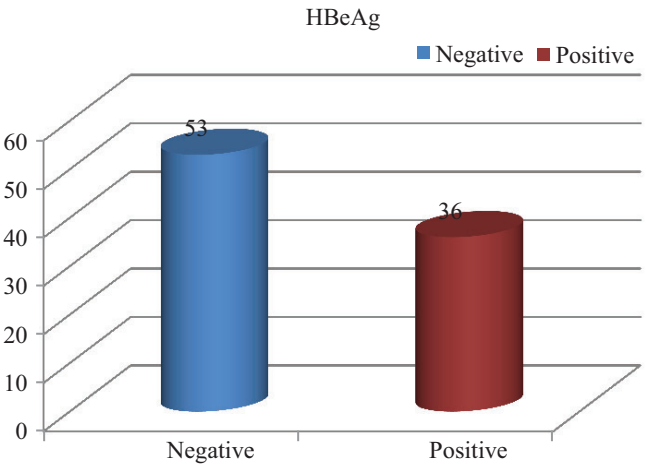

Figure-2: Showing HBeAg Positivity.

The presence of the HBeAg in the patients samples were determined by the cut-off value (0.125) that allowed the semi quantitative detection of the antigen.36(40.5%) sample had S/Co value >1.1 and were taken as positive, while as 53 (59.5%) samples were having S/Co value <0.9 were taken as negative (Figure 2).

Out of 36 HBeAg positive patients 27 (75%) were male and 9 (25%) were female patients suggesting that acute active hepatitis B infection rate higher in males than females

Only one sample out of 89 sample showed the optical density more than cutoff value and was considered positive for HDV-IgM suggestive of acute hepatitis D infection and that was a male patient .

DISCUSSION

Hepatitis D virus (HDV) is the smallest human virus. The presence and reproduction of HDV heavily depends on hepatitis B surface antigen. HDV infection is associated with a higher risk of cirrhosis and hepatocellular carcinoma compared with those who only have chronic Hepatitis B virus infection. Thus, early diagnostic intervention in HDV infected patients may be the right approach to avert end-stage liver disease and the development of cirrhosis.[64]

In a study in Naples (1972 and 1974) serum samples obtained from patients with acute hepatitis B were retrospectively evaluated, and for the first time, the IgM antibodiesagainst HDV was discovered and detected in more than 90% of cases. Most of the anti-HDV IgM-positive patients were also hepatitis B core Antigen (HBcAg) IgM-positive, suggesting an epidemic of HBV/HDV coinfection in Naples in those years.[10] The serum sample positive for Anti HDV IgM in our study was also found IgM anti-HBcpositive

HBeAg positivity has been seen in a lesser number of patients with HDV infection.[11] This finding is in agreement to the fact that in chronic HDV Infection HDV suppresses synthesis of HBV genome and gene products; but on the contrary, in our study we found that the patient positive for IgM-HDV was also positive for the HBeAg

In our study the total HBsAg positivity was 5.8%whichis a little high percentage as compared to national levels. The national scene has a decreased percentage of positivity after the introduction of HBsAg vaccination in the national immunization schedule. A higher level in our study can be attributed to the selection of only symptomatic patients suspected of viral hepatitis.

Earlier Chowdhury A et al[12] in 1997 had conducted a community based door to door epidemiological study in West Bengal and found an overall HBsAg carrier rate 5.3%

The anti-HDV positivity in acute viral hepatitis patients in our study was considerably low as compared to other studies in the country it varies from 10.7 to as high as >30 per cent.[13,14] In 1992, Amarapurkar et. al[14] from Mumbai had reported delta positivity in 16 per cent (23/148) of HBV-related AVH patients.

The seroprevalence of anti-HDV antibody in our study was 1.1%. This indicates the activity, by way of presence, of HDV infection in Kashmir.

In the current study, there was only one HDVIg M seropositive case & that too was a male. Analysis of the gender related seroprevalence of HDV antibody in various studies showed that females were more often infected than males (Pakistan[15] Babol, Iran.[16]

In this study the age of HDV positive patient was>50 years. In a study Shah Latika J et.al. (2012)[17], the cases of anti HDV antibody positivity is more with adults and older than 30 years of age which correlates well with our finding. Another study done in Pakistan by Asad U Khan[18] also has high prevalence in older (31.7%).

CONCLUSION

HDV affects individuals of all ages and various ethnic groups. HBV viral loads may be low, but rates of cirrhosis are higher in co infected patients and higher still in the tri-infected.

With no report on the overall prevalence and ramifications of hepatitis Delta virus (HDV) infection in this part of the world, the characteristics of chronic hepatitis B virus (CHB) patients co infected with HDV & rate of hepatitis C virus tri-infection were assessed in our study.

It has been found that the incidence of co infections is 1.1% indicating the presence of HDV infection in Kashmir valley. Though there was a HCV infected patient in our study group, it was not a case of tri-infection.

As such, health related medical bodies world over have no specific recommendation on hepatitis D, however prevention of HBV transmission by hepatitis B immunization, safe injection practices, blood safety, and harm reduction services with clean needles and syringes, are effective in preventing HDV transmission. People who are not immune to HBV (either by natural disease or immunization with the hepatitis B vaccine) are at risk of infection with HBV which puts them at risk of HDV infection.

Vaccination against HBV prevents HDV co infection, and hence expansion of childhood HBV immunization program as a measure to reduce hepatitis D incidence should be adopted vigorously. Also raising awareness, formulating evidence-based policy, preventing transmission, scaling up screening, care and treatment services should be used.

Our data suggests guidelines be set up for advocacy of HDV screening in all patients with HBV infection.

Studies such as ours should be taken up at the community level to ascertain the true dimensions of the problem as it is now established beyond doubt that the problem of co infection of HBV & HDV is there in this part of the world.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 24-12-2020; **Accepted:** 20-01-2021; **Published:** 18-02-2021