EDITORIAL

HEPATITIS D IN CHILDREN AND ADOLESCENTS – AN UPSURGE?

Sina Aziz

Pediatric liver disease due to viruses capable of sustained infection includes Hepatitis B virus (HBV) and Hepatitis C virus (HCV). HBV is a DNA virus and is transmitted through contamination with infected blood or body fluids and also mother to infant transmission. Seroprevalence of HBV is low in general pediatric population.[1] Recent data from Sarwar Zuberi Liver Centre (SZLC) shows an upsurge of HDV co infection with HBV in some areas of Sindh. However, the possibility exists that patients with HBV were not being screened for HDV, previously and now due to awareness among physicians HDV screening is also being done prior to starting treatment for HBV. Spontaneous rate of mother to infant transmission, so called vertical transmission for HBV is 85-90% which is much greater than other viruses such as HCV (4-6%).[2,3] This rate is in the absence of co-infection with HIV.

Hepatitis D virus or delta virus (HDV), the smallest known animal virus, is a defective RNA virus because it cannot produce infection without a concurrent HBV infection. The 36-nm-diameter virus is incapable of making its own coat protein; its outer coat is composed of excess HBsAg from HBV. Hence, the virion is a hybrid consisting of a nucleocapsid core, comprising HDV RNA genome and HDV antigen, and a lipid envelope containing HBsAg, and thus HDV infection occurs only in chronic HBV carriers.

HDV can cause an infection at the same time as the initial HBV infection (co infection), or HDV can infect a person who is already infected with HBV (super infection). The route of transmission is mainly parenteral: infection may occur at the same time or subsequent to HBV acquisition. Transmission usually occurs by intrafamilial or intimate contact in areas of high prevalence, which are primarily developing countries. HDV was assumed to be rare in the developing world. Very little data is available regarding the prevalence of HBV and HDV co infection in Pakistan. However, recently it has been documented as a co-infection with HBV in adult, and pediatric population from this part of the world also.[4-6] Patients' follow up at SZLC has shown that 50% of the patients presenting with HBV infection had a co infection of HBV and HDV. Treatment of HBV and HDV co infection requires a minimum, one year of expensive treatment which is not always possible in our group of low socio-economic patient population. This data is alarming as major risk factors in this study group were lack of HBV immunization and unsafe injection use. HDV genotype 1 was seen in our patients similar to other studies.[7] However; this aspect is being further explored. In areas of low prevalence, such as the United States, the percutaneous route of infection is far more common. HDV infections are uncommon in children in the United States but must be considered when fulminant hepatitis occurs. In the United States, HDV infection is found most frequently in parenteral drug abusers, developmentally disabled, patients with hemophilia and persons emigrating from areas that include southern Italy, parts of Eastern Europe, South America, Africa and the Middle East.[8]

HDV has diminished in Europe, since 1970-80s. However, HDV remains an important health problem outside Europe, with new foci of infection being identified in developing countries.[9] The incubation period for HDV super infection is about 2-8 weeks; with co-infection, the incubation period is similar to that of HBV infection.[10]

Liver pathology in HDV hepatitis has no distinguishing features except that damage is usually more severe.[11] In contrast to HBV, HDV causes injury directly by cytopathic mechanisms. Many of the more severe cases of HBV infection appear to be a result of co infection of HBV and HDV. HDV super infection of a person who has chronic HBV infection is more common in developed countries. Clinical presentation of HDV infection in HBV carriers may be asymptomatic with complete resolution of infection, develop acute hepatitis or fulminant hepatic failure, and develop rapid progression of chronic hepatitis. Symptoms

Correspondence: Dr. Sina Aziz, Associate Professor of Paediatrics,
Sarwar Zuberi Liver Centre, Dow University of Health Sciences, Karachi, Pakistan
E-mail: sigma_98@hotmail.com
Received: August 5, 2008: accepted; January 21, 2009

of HDV are similar to but usually more severe than those of other hepatotropic viruses. Clinical outcome of HDV infection depends upon the mechanism of infection. In acute hepatitis, which is more severe than for HBV alone, is common but the risk of developing chronic hepatitis is low. In super infection, acute illness is rare and chronic hepatitis is common. However, the risk of fulminant hepatitis is highest in super infection. HDV should be considered in any child who experiences acute hepatic failure. HBV/HDV co infection develop cirrhosis, hepatic decompensation, and HCC (hepatocellular carcinoma) compared to those with HBV alone.[12,13]

HDV infection can be detected by HDV antigen in hepatocyte by immunofluorescence or immunoperoxidase stains. HDV has not been isolated, and no circulating antigen has been identified. The diagnosis is made by detecting IgM antibody to HDV; the antibodies to HDV develop about 2-4 weeks after co infection and about 10 weeks after super infection. A test for anti-HDV antibody is commercially available. PCR assays for viral RNA are available.[12]

The prevention of HBV infection and eradication of chronic HBV carriage will prevent the disease associated with HDV infection. Treatment of HDV is not as yet optimum or satisfactory. However, RCT (randomized control trials) using IFN (interferon) monotherapy (dose from 3 to 9 million units (MU)) show a limited and variable response depending upon schedule of treatment.[14] However, therapeutic efficacy increases when high doses of IFN-á (5 MU daily or 9-10 MU three times weekly) are given for 12 to 24 months.[15]

In children the dose of alpha interferon is 6 MU/m^2 thrice weekly with a maximum dose of 10MU. Lamuvidine has been evaluated in a small number of patients and found to be in effective in inhibiting HDV replication.[16] At present no new therapies are available other than INF-á in the pediatric population. In very young children, less than 5 years of age, it is not advisable to use INF-á for HDV, due to side effects. Some trials are being done on PEG interferon.[12-17]

There is no vaccine for HDV. However, because HDV replication cannot occur without HBV co infection, immunization against HBV also prevents HDV infection. Hepatitis B vaccines and HBIG are used for the same indications as for Hepatitis B alone. Also, screening of HDV should be kept in mind for HBsAg positive patients especially before starting treatment for HBV. This is especially important as at SZLC, very young patients (7-10years of age) have been seen to be co infected with HBV and HDV.

REFERENCES

1. Aziz S, Muzaffar R, Hafiz S, Abbas Z, Zafar MN, Naqvi SA et al. Helicobacter pylori, hepatitis viruses a, c, e, antibodies and hbsag - prevalence and associated risk factors in pediatric communities of karachi. J Coll Physicians Surg Pak 2007; 17: 195-8.

2. Aziz S, Hossain N, Karim SA, Masheer S, Rajpar J, Soomro N et al. Occurrence & vertical transmission of HCV amongst low socio-economic pregnant population of Karachi XVIII FIGO world congress of Gynecology & Obstetrics, Malaysia 2006.

3. Jaffery T, Tariq N, Ayub R, Yawar A. Frequency of hepatitis C in pregnancy and pregnancy outcome. J Coll Physicians Surg Pak 2005; 15: 716-9.

4. Zuberi BF, Quraishy MS, Afsar S, Akhtar N, Kumar A, Dodani SK. Treatment outcome in patients of hepatitis B with hepatitis D: experience of 4 years at a tertiary care centre in Pakistan. J Coll Physicians Surg Pak 2007; 17: 320-2

5. Aziz S, Shabir S, Qamar R, Rajper J, Masroor M. Frequency and risk factors of hepatitis B and D among pediatric and adult patients presenting at a Tertiary Care Hospital of Karachi. (Abstract Book : World Congress of Pediatrics Gastroenterology, Hepatology, and Nutrition, Brazil; Auguest 16-20, 2008)

6. Zaki H, Darmstadt GI, Baten A, Ahsan CR, Saha SK. Seroepidemiology of hepatitis B and delta virus infections in Bangladesh. J Trop Pediatr 2003; 49: 371-4.

7. Moattar T, Abbas Z, Shabir S, Jafri W. Clinical presentation and genotype of hepatitis delta in Karachi. W J of Gastroenterol 2007; 14: 2604-7.

8. Ponzetto A, Forzani B, Parravicini PP Hele C, Zanetti A, Rizzetto M. Epidemiology of hepatitis delta virus (HDV) infection, Eur J Epidemiol 1985; 1: 257- 63.

9. Rizzetto M. Hepatitis D: the comeback? Liver Int 2009; 29: 140-2.

10. Abiad H, Ramani R, Currie JB. The natural history of hepatitis D virus infection in Illinois state facilities for the developmentally disabled.Am J Gastroenterol 2001; 96: 534-40.

11. Farci P. Delta Hepatitis: an update. J Hepatol 2003; 39: 212-9.

12. Lok AS, McMahon BJ. AASLD practice guidelines Chronic hepatitis B. Hepatology 2007; 45: 507-39.

13. Rizetto M, Durazzo M. Hepatitis Delta virus (HDV) infection: Epidemiological and clinical heterogeneity. J Hepatol 1991; 13: 116-8.

14. Chien RN. Current therapy for hepatitis C or D or immunodeficiency virus concurrent infection with chronic hepatitis B. Hepatol Int 2008; 2: 296-303.

15. Farci P, Roskaus T, Chessa L. Long term benefit of interferon á therapy of chronic hepatitis D: regression of advanced hepatic fibrosis. Gastroenterology 2004; 1740-9.

16. Yurdaydin C, Bozkaya H, Onder FO, Senturk H, Karaslan H, Akdogan M et al. Treatment of chronic delta hepatitis with lamivudine vs lamivudine + interferon vs interferon. J viral Hepat 2008; 15: 314-21.

17. Hoofnagle JH, Di Bisceglie AM. The treatment of chronic viral hepatitis. N Eng J Med 1997; 336: 347-56.