Hepatitis D in Pakistan
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World Hepatitis Day is observed every year on 28th of July. This year, the slogan of World Hepatitis Day was “Hepatitis, it’s closer than you think; know it, and confront it”. The key message of the day was that viral hepatitis is a preventable disease. While nearly everyone is susceptible, yet it rarely affects those who consciously guard against it. Pakistan is currently facing an epidemic of viral hepatitis in the country. Hepatitis B, C and D viruses share parallel routes of transmission. National prevalence of hepatitis B is 2.5%, and of hepatitis C is 4.8%. Currently, there are 15 million persons infected with this disease in the country. Hepatitis D virus or delta virus (HDV) is a small, defective RNA virus that can infect only individuals who have hepatitis B virus which acts as the carrier host. The prevalence of HDV antibodies in Pakistani hepatitis B surface antigen (HBsAg) positive individuals is approximately 16.6%. So there is a pool of at least 800,000 anti-HDV positive HBsAg positive individuals in the country.

The important trend in worldwide HDV infection is a global decline in the prevalence of hepatitis D infection. This decreasing trend is the result of global HBV vaccination, increasing awareness and improving preventive strategies in the developed countries. Approximately 5% of the global HBV cases are infected with HDV. Worldwide, more than 15 million people are co-infected with this virus. The areas of high endemicity for HDV have shifted from Southern Mediterranean region to less developed countries including Pakistan. The situation is alarming particularly in the rural Sindh.

Prevalence of anti-HDV antibodies in HBsAg positive patients visiting liver clinics or hospitals for treatment is very high. In one study, out of 362 HBsAg reactive patients tested for anti-HDV antibodies, 212 (58.6%) were found positive. A total of 65 anti-HDV positive patients were tested for the HDV RNA by PCR, out of which 30 patients (46.2%) had virus in their blood. The high prevalence districts were Kashmore, Jacobabad, Jaffarabad, Naseerabad, Quetta and Karachi. In other studies, anti-HDV antibodies were reactive in 45.3%, 35.2%, 34.9%, 31.5%, 26.8%, 23.6%, of HBsAg positive patients.

Since HDV infects hepatitis B virus (HBV) infected patients either as co-infection or as super-infection, hence both may have almost the same routes of transmission. Co-infection often leads to eradication of both agents, whereas super-infection mostly evolves to chronic hepatitis D. Worldwide, the highest prevalence is seen in certain groups including intravenous drug abusers, homosexual men and women, prostitutes, and people on haemodialysis. The infection can also spread by tattooing, body piercing by contaminated objects, sharing razors through barber services. There is a false belief among people of rural areas in the healing power of parenteral therapy particularly the use of injections and drips. This is a commonly employed practice in our country by general practitioners and quacks. Since male acquire these services more often in rural areas, they are more likely to be exposed to HDV.

Based on genomic variability, eight major genotypes of HDV have been identified, which differ as much as 40% in the nucleotide sequence. In Pakistan genotype-I is prevalent. Most patients suffering from hepatitis D are males and young adults. Not all the patients who are anti-HDV positive have circulating virus detectable by PCR in their blood. In one study, the amplification confirmed 30% samples to be HDV RNA positive. In another study, 46.2% tested positive for the virus. It means that a significant number of patients exposed to this virus in Pakistan either clear the virus or have very low level of viraemia. Most of the patients who have active HDV related disease are HBV DNA and HBeAg negative. Positive HDV antibody status is associated with higher transaminase levels compared to hepatitis-B mono-infection and suggests more severe and advanced disease. Severe inflammation in liver may lead to cirrhosis and hepatocellular carcinoma (HCC). Decreased liver size was noticed more in cases of HDV HCC compared with HBV mono-infection group where the liver size was normal or increased. HDV patients had lower platelets and larger varices on endoscopy.

Interferon alpha, standard or pegylated, is the only treatment option available. It does not seem to cure hepatitis D in most patients. The agent seems effective in suppressing viral and liver disease activity in some patients, but this improvement is not sustained in the majority of patients. In a systematic meta-analysis, standard interferon alpha led to end of treatment virological response in 32.6% of the patients compared with 7.8% in the untreated controls. Sustained virological response was achieved in 17.4% of patients.

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on interferon compared with 5.2% of controls. Use of standard interferon alpha is safe in children with HDV infection in terms of side effects and growth parameters. In a small local study, 80% (20/25) children and young adults were HDV-RNA negative after one year of treatment with standard interferon. Pegylated interferon alpha can lead to sustained HDV RNA elimination in about a quarter of patients.

HBV polymerase inhibitors are ineffective against HDV. A study evaluated safety and efficacy of 48 weeks of treatment with peginterferon alpha-2a plus adefovir, peginterferon alone, and adefovir alone. The efficacy of peginterferon, as judged by negative PCR, was sustained for 24 weeks after treatment in 28% of the patients receiving peginterferon plus adefovir or peginterferon alone; none of the patients receiving adefovir alone had negative results. Novel treatment options include prenylation inhibitors and HBV entry inhibitors which are currently in early clinical development. Liver transplantation is indicated in cases of liver failure, the facility is still in its initial phases of development in Pakistan.

Hepatitis D virus has infected a large number of patients with hepatitis B infection in Pakistan. Vaccinating the population against hepatitis B can prevent further spread of the infection. It is affecting young adults, rapidly leading to cirrhosis and its complications. The infection cannot be cured in majority of patients. It should be considered as one of the major public health problems of the country.

REFERENCES