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Hepatitis Delta-Like Viruses

Hepatit Delta-Benzeri Virüsler

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Dear Editor;

Hepatitis delta virus (HDV) is a unique defective ribonucleic acid (RNA) virus that requires the helper function of hepatitis B virus (HBV) for its life cycle. HDV-like viruses, also known as HDV-related agents, share similarities with HDV in terms of genomic organization, replication strategy, and pathogenicity. HDV was first discovered in 1977 as a satellite virus requiring the presence of HBV for replication. HDV is classified within the deltavirus genus and is unique in its reliance on HBV for packaging and transmission.

HDV is clearly distinguished from other viroids by its large genome and ability to encode proteins (1).

The origin and evolution of HDV are not fully understood. In recent years, HDV-like viruses that share genetic and functional similarities with HDV have been identified. These HDV-related agents exhibit analogous genomic structures and replication mechanisms, suggesting common evolutionary ancestry (1).

The combination of HDV and HBV infection is considered the most severe form of chronic viral hepatitis because of its more rapid progression toward liver-related death and hepatocellular carcinoma.

This editorial aims to provide a better understanding of HDV-like viruses, their molecular characteristics, epidemiological trends, clinical impact, and innovative therapeutic strategies.

HDV-like viruses possess a circular, single-stranded RNA genome associated with both forms of its only protein (large and small delta antigen or S- and L-HDAg), forming the viral ribonucleoprotein, similar to HDV. The genomic organization typically comprises a viroid-like structure with a single open reading frame encoding viral proteins. The replication strategy of HDV-like viruses involves the utilization of host cellular machinery and relies on the presence of HBV for its life cycle.

HDV is a defective virus and does not code for its own surface proteins; therefore, it uses the three forms of HBV surface proteins (small or S-HBsAg, medium or M-HBsAg and large or L-HBsAg) on which it depends to form its own envelope and egress and re-enter into hepatocytes (2).

During HDV replication in infected cells, two other main forms of viral RNA can be found: the antigenome, which is a replication intermediate and the exact complement of the genome sequence, and the HDV-mRNA coding for the two isoform of HDAg (2).

Worldwide, the number of HDV infections has decreased since the 1980s, mainly because of a successful global HBV vaccination program (3).

Understanding the global prevalence and distribution of HDV-like viruses is essential for assessing their public health impact. Epidemiological studies have revealed the presence of HDV-like agents in various geographical regions, emphasizing the need for continued surveillance and research.

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HDV affects nearly 5% of people who have a chronic infection with HBV.

Globally, the epidemic patterns of HDV infection and its contribution to the burden of liver disease are uncertain. A systematic review estimated that 12 million people worldwide have experienced HDV infection, with a higher prevalence in certain geographic areas and populations. The same evidence suggests that HDV is a significant contributor to HBV-associated liver disease (4).

HDV-like viruses are associated with a spectrum of clinical manifestations, including acute and chronic liver diseases.

HDV infection occurs when people become infected with both hepatitis B and D simultaneously (co-infection) or hepatitis D after first being infected with hepatitis B (super-infection). HDV co-infection with HBV is the most severe form of viral hepatitis, accelerating liver damage and increasing the risk of cirrhosis and liver cancer. Populations that are more likely to have HBV and HDV co-infection include indigenous populations, recipients of hemodialysis and people who inject drugs (3).

Accurate and timely diagnosis of HDV-like infections is crucial for patient management and public health interventions. Major diagnostic and therapeutic innovations have prompted the EASL Governing Board to commission specific Clinical Practice Guidelines on the identification, virologic and clinical characterization, prognostic assessment, and appropriate clinical and therapeutic management of HDV-infected individuals (4).

The unique characteristics of HDV-like viruses pose challenges in developing effective therapeutic interventions.

Hepatitis D infection can be prevented by hepatitis B immunization, but treatment success rates are low.

In cases of positivity, a subsequent step involves using reliable and validated quantitative HDV-RNA assays to confirm active infection. Timely and accurate assessment facilitated by validated serological biomarkers and non-invasive tests is crucial for effective diagnosis and risk stratification. Immunization against HBV is a potent preventive measure. Understanding viral-host-drug dynamics may help develop and optimize response-guided therapies for HDV patients (5,6).

HDV-like viruses, which resemble HDV in terms of genomic organization and replication strategies, represent an intriguing area of research within the virology field. Understanding their molecular characteristics, epidemiology, clinical impact, and therapeutic opportunities is essential for advancing our knowledge and developing targeted interventions against these emerging viral agents.

From a public health perspective and response, we need a better description of the HDV epidemic, standardized testing strategies, and better treatment options (1,4,6).

Addressing the complex challenges of HDV infection requires a multifaceted approach. Raising awareness among healthcare professionals and advocating reflex screening of HBV patients for anti-HDV antibodies is imperative.

Ethics

Authorship Contributions

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