

A Narrative Review on Chronic Hepatitis D Virus Infection and its Treatment

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Introduction

Hepatitis D virus is a defective RNA virus that requires hepatitis B virus for its replication and survival. Chronic hepatitis D is one of the most severe forms of viral hepatitis, characterized by rapid progression to liver cirrhosis and hepatocellular carcinoma. While global awareness of hepatitis B has led to significant advances in prevention and treatment, HDV infection remains a major global health challenge, with its clinical management remaining complex and limited by a lack of effective antiviral treatments. This narrative review provides an overview of chronic hepatitis D virus infection, its pathogenesis, clinical implications, and current treatment strategies, as well as emerging therapeutic options. Hepatitis D virus is unique in that it cannot infect the liver independently. It relies on hepatitis B virus for the production of its surface antigen, which is essential for the viral assembly and entry into hepatocytes. HDV infection occurs when an individual is co-infected or superinfected with HBV. In co-infection, the patient acquires both viruses simultaneously, while in superinfection, an individual with pre-existing chronic HBV infection acquires HDV later in life [1,2].

Description

Once inside the hepatocyte, HDV uses the HBV envelope proteins to enter the cell and replicate its RNA genome. The virus then produces its own hepatitis D antigen and replicates its genome in the nucleus. Chronic HDV infection leads to persistent inflammation, liver damage, and fibrosis, which increases the risk of cirrhosis and hepatocellular carcinoma. The immune response in HDV infection is more intense than in other forms of viral hepatitis, contributing to significant liver injury. The host's immune response, while attempting to clear the infection, often leads to chronic inflammation, fibrosis, and eventual liver failure. The immune-mediated liver damage is the primary factor driving the progression of HDV-related diseases. HDV can cause both acute and chronic infections. Acute HDV infection often presents with the typical symptoms of viral hepatitis, including fatigue, jaundice, abdominal pain, and elevated liver enzymes. However, chronic HDV infection can evolve from either a co-infection or a superinfection, with the majority of cases eventually progressing to chronic disease. Chronic hepatitis D is often asymptomatic in its early stages, and liver damage may progress silently. As the infection advances, patients may develop symptoms related to liver dysfunction, including portal hypertension, ascites, and gastrointestinal bleeding, which are common complications of cirrhosis. Patients with chronic HDV infection are at a significantly higher risk of developing liver cirrhosis and hepatocellular carcinoma compared to those with HBV mono-infection. The presence of HDV exacerbates the inflammatory response in the liver, leading to more rapid fibrosis progression [3-5].

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Conclusion

Chronic hepatitis D virus infection is a severe and potentially life-threatening disease that significantly accelerates liver damage in those co-infected with HBV. While treatment options remain limited, the approval of bulevirtide marks an important step forward in the management of HDV. However, further research is needed to develop more effective therapies, improve patient outcomes, and reduce the risk of liver-related complications such as cirrhosis and hepatocellular carcinoma. As our understanding of HDV pathogenesis and therapeutic strategies evolves, there is hope that more effective and accessible treatments will become available in the near future. In patients with end-stage liver disease due to chronic HDV infection, liver transplantation may be considered. However, HDV can recur in the transplanted liver, and the risk of recurrence is higher in patients who are not adequately treated for HDV before transplantation. Liver transplantation is typically a last resort for individuals with decompensated cirrhosis or HCC resulting from chronic HDV infection.

Acknowledgement

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Conflict of Interest

None.

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