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Review Article

Hepatitis E Virus: Understanding Transmission, Zoonotic Impacts, and Global Health Challenges

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Abstract

The hepatitis E virus (HEV) is a global health issue, particularly in regions where it is endemic, accounting for over half of all acute viral hepatitis cases. HEV is zoonotic, with animals such as swine, rabbits, deer, and rodents serving as reservoirs. This virus is primarily transmitted via the fecal-oral route through contaminated water and food, leading to outbreaks in areas with poor sanitation. Human-to-human transmission is rare, but other routes, including blood transfusions and vertical transmission from mother to fetus, are increasingly recognized, contributing to high stillbirth rates in developing countries. Moreover, HEV infections vary from asymptomatic to severe, potentially resulting in fatal fulminant hepatic failure. Immunocompromised individuals, such as organ transplant recipients, are at heightened risk of persistent infections that can progress to cirrhosis. Diagnosis relies on molecular methods (PCR) and serological assays (ELISA) for detecting HEV RNA and identifying anti-HEV antibodies, respectively. Birds, rabbits, and bats serve as reservoirs. Human HEV cases are mainly linked to genotypes 3 and 4, with primary reservoirs being domestic swine, wild boar, and deer. In addition, transmission can occur through direct animal contact, environmental contamination, organ transplants, and blood transfusions. Preventive measures focus on improving sanitation in developing regions while avoiding raw or undercooked animal products in developed countries. Studies demonstrate varying HEV seroprevalence among animals across different regions, highlighting the importance of understanding specific risk factors for transmission. Overall, HEV is a serious global health threat, with effective control and prevention requiring sustained research, improved sanitation, and comprehensive surveillance efforts.

Keywords: Hepatitis E virus, Zoonotic transmission, Fecal-oral route, Immunocompromised individuals, HEV vaccine development

Introduction

Hepatitis E virus (HEV) poses a major global health challenge and is the leading cause of enterically transmitted hepatitis in endemic areas, affecting over half of acute viral hepatitis cases. Approximately one-third of the worldwide population (nearly two billion people) live in HEV-endemic regions and are at risk of infection.[1,2] Hepatitis E was first characterized by Balayan et al in 1983 [3], with the HEV genome isolated and cloned in 1990.[4] In addition, the first serological assay for HEV antibodies was developed in 1991.[5] In developing countries, HEV outbreaks are primarily waterborne due to contaminated water and poor sanitation.[6,7] In contrast, developed countries, including the USA, Japan, and Europe, witness sporadic HEV cases, often linked to travel to endemic regions.[7] The zoonotic nature of this virus is distinct among hepatitis viruses, with various animals, including swine, rabbits, deer, and rodents, serving as reservoirs.[8,9] HEV transmission mainly occurs through the fecal-oral route, with contaminated water and food as common vectors.[10] Although human-to-human transmission is rare, other routes (e.g, blood transfusions and vertical transmission from mother to child) are gaining recognition.[11,12]

HEV can cause a spectrum of illnesses from asymptomatic to severe, including fulminant hepatic failure.[13] Immunocompromised individuals (e.g., transplant recipients) are at higher risk of chronic HEV infection, which can progress to cirrhosis.[14,15] The laboratory diagnosis of HEV includes molecular techniques (e.g., polymerase chain reaction) for detecting HEV RNA and serological assays (e.g., enzyme-linked immunosorbent assay) for anti-HEV antibodies.[8,16,17] Preventive measures emphasize enhancing sanitation and surveillance, especially in high-risk populations. In addition, avoiding raw or undercooked animal products in developed countries can reduce zoonotic transmission.[18] A vaccine for HEV produced in China shows promise, particularly for genotypes prevalent in endemic regions, though its efficacy against other genotypes is still being studied.[19,20]

Zoonotic Significance

Identifying HEV in domestic pigs in the USA in 1997 marked the discovery of its zoonotic strain.[21] Various animal species (e.g., birds, rabbits, rats, fish, bats, and camels) have been identified as HEV reservoirs.[22,23] Most human HEV cases are related to genotypes 3 and 4, which are zoonotic, with primary reservoirs being wild boar, domestic swine, and deer.[24-26] HEV can also be transmitted through organ transplants, environmental contamination, blood transfusions, and direct contact with animals.[27] Immunocompromised individuals are at higher risk of persistent HEV infection and extrahepatic complications. Other animal strains, including those from rabbits and rats, have also been associated with human diseases.[28]

Prevention and Control

Preventing HEV in developing regions involves improving sanitation to prevent fecal-oral transmission. In developed countries, avoiding raw or undercooked animal products prevents zoonotic transmission. The World Health Organization provides guidelines to manage waterborne HEV outbreaks.[18] A prophylactic vaccine for HEV developed in China shows promise for preventing the disease, particularly in endemic regions. The effectiveness of the vaccine against various HEV genotypes is still under evaluation.[19,20]

Prevalence

In one study, HEV seropositivity was the highest in female dogs (26.0%), followed by male cats (20.4%), male dogs (15.9%), and female cats (15.2%), with no significant differences between these groups.[29] Moreover, the prevalence of anti-HEV antibodies varied by age, with no remarkable differences across age groups.[29] However, HEV seroprevalence in animals noticeably differed across regions and species, with some studies demonstrating higher rates in dogs and cats in certain countries than others. In Bulgaria, dogs, cats, horses, cattle, sheep, and goats showed a seroprevalence of 21.1%, 17.7%, 8.3%, 7.7%, 32.2%, and 24.4%, respectively.[29] These findings contribute to understanding HEV prevalence in various animal populations.

Additionally, some studies reported that male animals [30-36] and older age groups tend to have higher HEV seroprevalence.[30,35,37,38] Various factors, including breed and environmental conditions, influence HEV infection rates in dogs.[39] In China, urban stray dogs displayed higher infection rates than pet and farm dogs [39], highlighting the importance of understanding specific risk factors for HEV transmission among animal populations.

Conclusion

As mentioned, HEV is considered a serious health challenge worldwide and a leading cause of acute viral hepatitis. The initial identification of the HEV occurred in 1983, with subsequent isolation and cloning of its genome achieved in 1990. HEV primarily disseminates through the fecal-oral route, with contaminated water serving as the principal transmission vector in developing countries, often resulting in large-scale outbreaks. Conversely, sporadic cases predominate in industrialized nations. HEV is a zoonotic pathogen with a broad animal host range, posing a serious risk to human health, particularly among pregnant women who experience severe disease progression. Moreover, HEV is primarily transmitted via the fecal-oral route through contaminated food and water, frequently presenting clinically similar to hepatitis A. Immunocompromised individuals are susceptible to persistent HEV infection, which can progress to cirrhosis. A promising HEV vaccine has been developed in China, offering hope for preventing this serious global health burden. However, sustained research and comprehensive surveillance efforts remain indispensable for effectively controlling this virus.

Author Contribution

Amir Mohammad Naghshe Javaheri: Writing-Original draft
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Competing Interests

The authors declare that there is no conflict of interest.

Data availability statement

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Ethical Approval

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a review article with no original research data.

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