APMB - Atti della Accademia Peloritana dei Pericolanti
Classe di Scienze Medico Biologiche
Vol. 108(1) 2020

ISSN 1828-6550

DOI: 10.6092 / 1828-6550 / APMB. 108.1.2020. SD3

Scholarly Dialogs SD3 (1-5)

Hepatitis e virus seroprevalence in farmed animals: a public health risk

[1]Michela Pugliese, [1]Rocky La Maestra, [1]Pietro Paolo Niutta

[1]Department of Veterinary Sciences, University of Messina, Italy

Abstract

Hepatitis E virus (HEV) is a zoonotic virus typically associated with acute self-limited or fulminant hepatitis in humans. The disease transmitted by oral-fecal route is endemic in many developing countries where sanitation conditions are suboptimal. In industrialized countries, the transmission occurs from animals to humans by the consumption of contaminated water, raw/undercooked animal products or inner organs.The swine is the most important reservoir of HEV zoonotic transmission, but the high seroprevalence of HEV in other animals indicates a theirpotential role in the transmission of disease. Indeed, the high sequence similarity between cattle, sheep, swine, and human populations suggests a complicated interspecies transmission. The aim of this review is to detail the current knowledge of the HEV in farmed animals, focusing on their role in the transmission of HEV.

KeyWords: Hepatitis E, farmed animals, foodborne transmission, zoonosis, genotype

Corresponding Author: Michela Pugliese - mpugliese@unime.it

Introduction

The HEV represents, in addition to hepatitis A, B, C and D viruses, one of the five majors human hepatotropic viruses. In most human patients symptoms are similar to mild/moderate influenza which persists for a few weeks. In other cases, symptoms may be more severe occurring fever, nausea, abdominal pain, vomiting, anorexia, and hepatomegaly (1). The HEV mortality rate in healthy humans is generally low (0.2–0.3%). However, in rural countries where HEV is endemic, the case fatality rate increases until 20-30% in pregnant women and immunocompromised patients (2). In past years, the potential nature zoonotic for some genotypes of HEV was identified. In this review, the Authors detail the current knowledge of the HEV in farmed animals, focusing on the role of these animals in the transmission of HEV.

Methods

A systematic analysis using the PubMed electronic database for English language abstracts and full-text articles published between 2009 and January 2019 was performed. The search terms included: “hepatitis E zoonosis”, “viral hepatitis in farmed animals”, “HEV and farmed animals”, “farmed animal and hepatitis E”, “transmission foodborne”.

Virus biology and transmission

Hepatitis E virus (HEV) is a small non-envelope RNA single strand virus with a positive polarity, belongs to the family of *Hepeviridae*, genus *Orthohepevirus* and species *Orthohepevirus*A (3).

HEV presents seven major genotypes: genotypes 1 and 2 infect only humans, while genotypes 3 and 4 may infect humans, pigs, cows, rabbits, deer, and mongoose. Genotypes 5 and 6 include strains isolated from wild boar, whereas the genotype 7 has been isolated from camel (4).

Viral factors, host factors and, the transmission route are considered important variables in the infectivity of the virus. Indeed, it is reported that same viral doses induced variations in the overall course of the disease (5). Experimental infections have demonstrated that HEV is transmissible between nonhumans primates to animals, suggesting a potential role of different animals in the diffusion of HEV (6). In rural countries, where genotypes 1 and 2 of are transmitted via contaminated water, the diffusion of HEV is maintained by infected individuals with clinical or subclinical signs, who contaminate water supplies (7). Conversely, in developed countries, where most cases of HEV infection are locally acquired, the importance of animal reservoirs plays an important role. The swine are considered the main reservoir for genotypes 3 and 4, but the HEV seroprevalence in other species of animals such as cows, sheep, goats, wild boar, deer, and rabbits contribute to diffuse the virus in humans (8).

Diagnosis of HEV infection

The diagnosis of HEV requires a combination of molecular and serological tests that can be used to detect viral proteins and/or genome. The detection of serum anti-HEV antibodies by double-antibody sandwich enzyme immunoassay (ELISA) techniques is used commonly (9). Commercial enzyme immunoassays and rapid immunochromatographic kits based on ORF2/ORF3 peptides can detect the presence of IgM or IgG antibodies induced by the four major genotypes of HEV (10). No cross-reactivity of HEV antigen with other viruses has been documented. The exact period of the anti-HEV IgG antibody detection is unknew.

Real-time PCR is considered the gold standard for HEV diagnosis. Compared to conventional PCR, real-time PCR minimizes cross-contamination between samples (11). RNA detection is a sole method for the identification of HEV genotypes or sub-genotypes. Different molecular assays have been commercialized for HEV RNA detection with variable differences in sensitivity and specificity.

HEV in farmed animals

Serological and/or molecular analyses have been well-documented the presence of HEV in different animal species such as farmed animals, pets, laboratory animals, wild animals or zoo

animals (4). The swine has indicated as a major true animal reservoir (12). In other animal species, HEV has observed with a lower prevalence suggesting the presence of spillover infections. The anti-HEV seroprevalence in swine is usually higher (23-100%) than other animals, with an increase of serum positivity related to the age (13). In China, a country considered endemic for HEV, there is high seropositivity of farmed animals (pigs over 80%) and slaughterhouse workers, who show a consistently higher seroprevalence compared to the control group of people, suggesting that even direct contact with infected animals can transmit the disease (14).

The seroprevalence of HEV in swine, sheep, cattle, horse, milk cow, rabbit, duck, and chicken indicates that the contact with these animals may be considered a potential risk factor of HEV transmission to humans (4), but the complete range of species that may be considered reservoirs is unknown. Few studies are reported HEV-specific antibodies detection in different breeds of domestic cattle (*Bostaurusprimigenius*) like yellow cattle (15), Holstein Frisian cattle (16) and other dairy cattle as well as in domesticated wild bovids, such as yak (*Bosgrunniens*) (17), buffalo (*Synceruscaffer*) (18) or bison (*Bison bison*) (19). HEV-4 strains have been identified in Holstein cows kept on mixed farms together with pigs in Southwest China and in yellow cattle from Eastern China (20). HEV-specific antibodies in cattle of 4.4%–6.9% in India, 1.4% in Brazil, 10.4% to 37% in China and up to 15% in the USA (4) have been reported.

HEV-specific antibodies have also been found in goat (*Capra hircusaegagrus*) and sheep (*Ovisaries*). A study has documented seropositivity rates ranged between 9.4% and 4.4% for goat and sheep in Egypt (21). Similarly, in Italy HEV-3 strains have been documented in 9.24% of goats (22). In Spain, specific IgG antibodies have been found in 0.6% and 1.92% of goats and sheep, respectively (23). In the USA and in Eastern China 16% of domesticated farmed goats have been found positive for anti- HEV IgG antibodies (24). In addition, 11.43% of sheep were positive for HEV- RNA (25).

Data involving the prevalence of HEV antibodies in rabbits farmed for meat consumption are consistent. In USA a IgG seroprevalence of 36.5% has been reported (26). In China an IgG seroprevalence between 55% and 57% has been reported (27). HEV- RNA was detected in 7.5% (serum) and 7.0% (feces) of rabbits (28). Additionally, HEV- RNA was detected in 5% of Japanese White rabbits and Rex rabbits from China (29). A prevalence of 7% has been documented in liver specimens of rabbits, slaughtered for consumption in France specimens (30). Rabbit HEV is associated with genotype 3 but present a different subtype. This subtype has been recently also described in a few human patients from France (31).

Conclusions

HEV is an infection with contrasting aspects. They are not completely clear the specific factors that have determined an increase of cases in industrialized countries.

The role of domestic animals such as cattle, sheep, and goats, or other animals for HEV transmission to human requests to be investigated detailly. It is needed to evaluate the risk of zoonotic transmission of HEV from these animals and to mature active protection plans for the public in contact with the animals.

Conflicts of Interest: There is no potential conflict of interest, and the authors have nothing to disclose. This work was not supported by any grant

References

1. Labrique, A., Kuniholm, M.H., Nelson, K. (2010). The global impact of hepatitis E: new horizons for an emerging virus, 53–93. In: Scheld, W.M., Grayson, M.L., Hughes, J.M. (ed.), Emerging infections, 9th ed., A.S.M. Press, Washington, D.C.
2. Farshadpour, F., Taherkhani, S., Taherkhani, R.. (2019). Hepatitis E Virus Infection During Pregnancy: The Overlooked Cause of Maternal and Fetal Mortality. Infect Disord Drug Targets,19(3), 334-336.
3. Smith, D.B., Simmonds, P., Jameel, S., Emerson, S.U., Harrison, T.J., Meng, X.J., Okamoto, H., Van der Poel, W.H., Purdy, M.A. International Committee on Taxonomy of Viruses Hepeviridae Study Group. (2014). Consensus proposals for classification of the family Hepeviridae. J Gen Virol, 95, 2223–2232.
4. Spahr, C., Knauf-Witzens, T., Vahlenkamp, T., Ulrich, R.G., Johne, R. (2018). Hepatitis E virus and related viruses in wild, domestic and zoo animals: A review. Zoonoses Public Health, 65, 11-29.
5. Holla, R.P., Ahmad I., Ahmad Z., Jameel, S. (2013). Molecular virology of hepatitis E virus. Semin Liver Dis, 33, 3-14.
6. Graff, J., Nguyen H., Yu C., Elkins, W.R., St Claire, M., Purcell, R.H., Emerson, S.U. (2005).The open reading frame 3 gene of hepatitis e virus contains a cis-reactive element and encodes a protein required for infection of macaques. J Virol, 79, 66806689.
7. Aggarwal, R., Goel, A. (2016). Advances in hepatitis E - I: virology, pathogenesis and diagnosis. Expert RevGastroenterolHepatol, 10, 1053–1063.
8. Donnelly, M.C., Scobie, L., Crossan, C.L., Dalton, H., Hayes, P.C., Simpson, K.J. (2017). Review article: hepatitis E - a concise review of virology, epidemiology, clinical presentation and therapy.Aliment PharmacolTher, 46,126-141.
9. Engle, R.E., Yu, C., Emerson, S.U., Meng, X.J., Purcell, R.H. (2002). Hepatitis E virus (HEV) capsid antigens derived from viruses of human and swine origin are equally efficient for detecting anti-HEV by enzyme immunoassay. J ClinMicrobiol, 40, 4576–4580.
10. Zhang, F., Li, X., Li, Z., Harrison, T.J., Chong, H. (2006). Detection of HEV antigen as a novel marker for the diagnosis of hepatitis E. J Med Virol, 78, 1441–1448.
11. Baylis, S.A., Blumel, J., Mizusawa, S., Matsubayashi, K., Sakata, H., Okada, Y., Nübling, C.M., Hanschmann, K.M., HEV Collaborative Study Group. (2013). World Health Organization International Standard to harmonize assays for detection of hepatitis E virus RNA. Emerg Infect Dis, 19, 729-735.
12. Doceul, V., Bagdassarian, E., Demange, A., Pavio, N. (2016). Zoonotic hepatitis E virus: Classification, animal reservoirs and transmission routes. Viruses, 8(10), 270.
13. Caruso, C., Peletto, S., Rosamilia, A., Modesto, P., Chiavacci, L., Sona, B., Masoero, L. (2016). Hepatitis E virus: A cross- sectional serological and virological study in pigs and humans at zoonotic risk within a high- density pig farming area. TransboundEmerg Dis, 64, 1443–1453.
14. Yan, B., Zhang, L., Gong, L., Lv, J., Feng, Y., Liu, J., Xu, A. (2016). Hepatitis E virus in Yellow Cattle, Shandong, Eastern China. Emerg Infect Dis, 22(12), 2211–2212.
15. Huang, F., Li, Y., Yu, W., Jing, S., Wang, J., Long, F., Pan, Q. (2016). Excretion of infectious hepatitis E virus into milk in cows imposes high risks of zoonosis. Hepatology, 64(2), 350–359.
16. Xu, F., Pan, Y., Baloch, A.R., Tian, L., Wang, M., Na, W., Zeng, Q. (2014). Hepatitis E virus genotype 4 in yak, northwestern china. Emerg Infect Dis, 20(12): 2182–2184.
17. El-Tras, W.F., Tayel, A.A., El-Kady, N.N. (2013). Seroprevalence of hepatitis E virus in humans and geographically matched food animals in Egypt. Zoonoses and Public Health, 60, 244–251.
18. Dong, C., Meng, J., Dai, X., Liang, J.H., Feagins, A.R., Meng, X.J., Teo, C.G. (2011). Restricted

enzooticity of hepatitis E virus genotypes 1 to 4 in the United States. J ClinMicrobiol, 49(12), 4164–4172.
19. Di Martina, B., Di Profio, F., Melegari, I., Sarchese, V., Robetto, S., Marsilio, F., Martella, V. (2016). Detection of hepatitis E virus (HEV) in goats. Virus Res, 225, 69–72.
20. Huang, F., Li, Y., Yu, W., Jing, S., Wang, J., Long, F., Pan, Q. (2016). Excretion of infectious hepatitis E virus into milk in cows imposes high risks of zoonosis. Hepatology, 64(2), 350–359.
21. El-Tras, W.F., Tayel, A.A., El-Kady, N.N. (2013). Seroprevalence of hepatitis E virus in humans and geographically matched food animals in Egypt. Zoonoses and Public Health, 60, 244–251.
22. Di Martina, B., Di Profio, F., Melegari, I., Sarchese, V., Robetto, S., Marsilio, F., Martella, V. (2016). Detection of hepatitis E virus (HEV) in goats. Virus Res, 225, 69–72.
23. Peralta, B., Casas, M., de Deus, N., Martín, M., Ortuno, A., Pérez-Martín, E., Mateu, E. (2009). Anti-HEV antibodies in domestic animal species and rodents from Spain using a genotype 3- based ELISA. Vet Microbiol, 137, 66–73.
24 Sanford, B. J., Emerson, S.U., Purcell, R.H., Engle, R. E., Dryman, B.A., Cecere T.E., Meng, X.J. (2013). Serological evidence for a hepatitis E virus- related agent in goats in the United States. TransboundEmergDis, 60(6), 538–545.
25. Kenney,S.C. (2019). The Current Host Range of Hepatitis E Viruses. Viruses, 11(5), 452.
26. Cossaboom, C.M., Córdoba, L., Dryman, B.A., Meng, X. (2011). Hepatitis E virus in rabbits, Virginia, USA. Emerg Infect Dis, 17(11), 2047–2049.
27. Geng, J., Wang, L., Wang, X., Fu, H., Bu, Q., Zhu, Y., Zhuang, H. (2011). Study on prevalence and genotype of hepatitis E virus isolated from Rex Rabbits in Beijing, China. J ViralHepatitis, 18(9), 661–667.
28. Xia, J., Zeng, H., Liu, L., Zhang, Y., Liu, P., Geng, J., Zhuang, H. (2015). Swine and rabbits are the main reservoirs of hepatitis E virus in China: Detection of HEV RNA in feces of farmed and wild animals. ArchivVirol, 160, 2791–2798.
29. Zhao, C., Ma, Z., Harrison, T.J., Feng, R., Zhang, C., Qiao, Z., Wang, Y. (2009). A novel genotype of. Hepatitis E virus prevalent among farmed rabbits in China. J MedVirol, 81, 1371–1379.
30. Abravanel, F., Lhomme, S., El Costa, H., Schvartz, B., Peron, J. M., Kamar, N., Izopet, J. (2017). Rabbit hepatitis E virus infections in humans, France. Emerg Infect Dis, 23(7), 1191–1193.
31. Izopet, J., Dubois, M., Bertagnoli, S., Lhomme, S., Marchandeau, S., Boucher, S., Guérin, J.L. (2012). Hepatitis E virus strains in rabbits and evidence of a closely related strain in humans, France. EmergInfectDis, 18(8), 1274–1281.

©2020by the Author(s); licensee Accademia Peloritana dei Pericolanti (Messina, Italy). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

Communicated and received Dec 10, 2019, revised and accepted March 26, 2020, published on line June 15 2020