

Swine enteric viruses: A potential zoonotic threat

Vaishali¹, M. Kumar², S. Kumari^{3*}, S. Kumar⁴, A. Dalal⁵

¹ Department of Veterinary Public Health and Epidemiology, RAJUVAS, Bikaner, Rajasthan; ²Department of Veterinary Public Health and Epidemiology, ³Livestock Farm Complex, ⁵Department of Veterinary Microbiology, LUVAS, Hisar, Haryana; ⁴CVH, Mandvi, Moonak, Punjab, India

*Correspondence author email: drsonughadwal@gmail.com

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Abstract

Zoonotic transmission of swine enteric viruses presents a critical public health challenge, exacerbated by the close association between humans and pigs. Swine serve as reservoirs for various zoonotic pathogens, including viral agents like rotavirus, astrovirus, hepatitis E, and picobirna viruses, which can lead to significant economic and health impacts. This review explores the epidemiology and zoonotic potential of these swine enteric viruses, emphasizing the importance of understanding their transmission dynamics and molecular characteristics. Notably, viruses such as rotavirus and astrovirus are prevalent in swine populations globally, with evidence of cross-species transmission to humans, leading to gastrointestinal illnesses and substantial economic losses due to reduced livestock productivity and trade restrictions. Hepatitis E virus, with its capacity for zoonotic transmission, underscores the necessity of monitoring swine populations for potential public health threats. Moreover, the detection of genetically similar picobirnaviruses in both humans and swine highlights the need for further research into the mechanisms of interspecies transmission and the development of effective control measures.

Keywords: Zoonotic transmission; Swine enteric viruses; Astrovirus; Rotavirus; Hepatitis E virus

Introduction

Zoonoses, as defined by the World Health Organization (WHO) Expert Committee on Zoonoses in 1951, are diseases and infections that are naturally transmitted between vertebrate animals and humans. As per the World Organization for Animal Health (WOAH), approximately 60% to 75% of the pathogens responsible for human infections and emerging diseases have their origins in animals (Libera et al., 2022). The emergence of zoonotic disease in humans commenced following the advent of agriculture and the domestication of animals, a period during which humans began to coexist in significant numbers and close proximity to various vertebrate animals. The pathogens that are responsible for these zoonotic illnesses raise a significant public health alarm.

Pigs have helped to uplift the economic conditions of weaker section in developing countries (Das et al., 2012) but they have also been recognized as a reservoir for numerous zoonotic pathogens that can be transmitted to humans (Aguilera et al., 2024). Some of the agents are foodborne and can result from the feco-oral route of contamination. In addition to bacteria (*Escherichia coli* etc.), and parasites (*Giardia*, *Entamoeba*, *Cryptosporidium*, etc.), pigs also host a diverse array of viruses in their digestive system (Influenza A Virus, Porcine Endogenous Retrovirus, etc.), some of which may not induce illness in the animals themselves (Machnowska et al., 2014).

Viral gastroenteritis is one of the major problems that results in diarrhea and is a serious public health issue that has a negative impact causing heavy mortality and high economic losses (Malik et al., 2014). Young piglets are particularly vulnerable to the disease, and the virus's rapid spread within a confined environment like a pig farm can exacerbate the problem. The disease can lead to reduced growth rates and poor weight gain even for pigs that survive the infection. This can delay the time it takes for the pigs to reach market weight, affecting the overall productivity and profitability of piggery (Vaishali et al., 2023). The outbreaks of viral gastroenteritis have the potential to disturb the regular production timelines and breeding programs. To contain the spread, it might be essential to implement quarantine protocols and reduce the population in affected areas. These measures can result in added expenses and production delays.

Viral gastroenteritis tends to impact the broader economy resulting in trade restrictions and bans imposed by importing countries. The reduced supplies of pork due to disease-related mortalities can lead to price fluctuations in the domestic market. The presence of these diseases often results in trade restrictions and bans imposed by importing countries. When outbreaks occur, the reduced supply of pork and other livestock products due to disease-related mortalities can lead to price fluctuations and instability in the domestic market. The economic impacts can be far-reaching, affecting producers, processors, and consumers through disruptions in the supply chain and price volatility (Brnic et al., 2023).

The most common zoonotic viral enteric viruses responsible for causing gastrointestinal infections are rotavirus, astrovirus, circovirus, picobirnavirus, norovirus, hepatitis E, porcine epidemic diarrhea virus, porcine transmissible gastroenteritis virus, sapelovirus, kobuvirus (Malik et al., 2014a). Even though swine enteric viruses are common and don't show clinical symptoms that can have notable economic and public health consequences, they are frequently neglected, and there remains a shortage of information regarding their spread and the mechanisms by which they cause disease.

The present review sheds light on swine enteric viruses, emphasizing their potential for zoonotic transmission, supported by findings from molecular epidemiological investigations.

Porcine Rotavirus A

Rotavirus is a double-stranded RNA virus belonging to the family *Reoviridae*, it has a triple-layered protein cascade surrounding its genome which entails 11 segments encoding six structural proteins (VP1-VP4, VP6, and VP7) and five non-structural proteins (NSP1-NSP5/6). Rotaviruses are distinctly divided into 10 groups or species (RVA to RVC, RVE, RVH, RVI and RVJ) in both animal and human hosts, based on VP6 gene (Ferrari et al., 2022). The prevalence of rotavirus is evidenced throughout the globe including Africa, America, Europe, and Asia including India as described in Table 1. Among all the gastrointestinal viruses, rotaviruses are the leading cause of diarrhea afflicting heavy economic losses and the outbreak of rotavirus is most commonly seen among piglets from 2-4 weeks of age (Abass et al., 2022).

In terms of epidemiology, Rotavirus A is a significant enteric pathogen which primarily causes diarrhea in both animals and humans and has a possibility of zoonotic transmission. RVA possesses the capacity for zoonotic transmission, indicating significant genetic parallels between strains found in humans and animals, particularly highlighted through comprehensive genome sequencing (Neira et al., 2023). Various epidemiological studies have shown multiple genotypes of RVA shared by both humans and pigs sharing high genetic similarity, suggesting interspecies transmission (Flores et al., 2021; Wu et al., 2022). Genetic typing has also revealed a relationship between pig and human isolates, indicating zoonotic transmission between pigs and humans. Although evidence supports zoonotic transmission of rotaviruses, the exact pathways of transmission between animal and humans remain unclear (Salamunova et al., 2020).

Porcine astrovirus

Astroviruses (AstVs) represent significant viral agents responsible for diarrhea in both human infants and various animal species, presenting a threat to public health and imposing economic burdens, and are significant enteric viruses following rotavirus. Family *Astroviridae* has two genera: *Avastrovirus* (AAstV) infecting avian hosts such as chicken, turkey, ducks, guinea fowls, and pigeons, and *Mamastrovirus* (MAstV) infecting a wide range of mammalian hosts, including humans, rats, pigs, cheetahs, mink, sheep, marine mammals, rabbits, dogs, cattle, bats, and deer. They are icosahedral, single-stranded, positive-sense RNA viruses with a genome ranging from 6-8 kb, exhibiting a distinctive star-like appearance due to protruding capsid spikes (Chu et al., 2008).

Porcine astrovirus has a wide range and diverse reviews have cautioned about more than one genotype (PAstV1-5) of porcine astrovirus circulating inside the swine population, which serves as a reservoir for some zoonotic diseases (Reuter et al., 2011). PAstV infections are commonly found in the pig population worldwide, and are associated with severe clinical signs involving, diarrhea, vomiting and reduced weight gain. Some of the symptoms include encephalitis or disseminated infections (Boros et al., 2017). PAstV are responsible for causing mild to severe gastroenteritis and has been reported in both healthy and diarrheic pigs (Matias Ferreyra et al., 2020).

The epidemiological studies have shown that PAstV infections are widespread globally in the pig population. Molecular detection and genetic characterization of this virus have been reported from different countries including China (Xiao et al., 2017), Czech Republic, Germany, Africa, Hungary, Japan, Slovakia, Sweden, South Korea, Thailand, United States, and India (Dufkova et al., 2013; Machnowska et al., 2014; Amimo et al., 2014; Boros et al., 2017; Ito et al., 2017; Salamunova et al., 2018; Karlsson 2016; Kumthip et al., 2018; Vaishali et al., 2023).

In India, the prevalence of porcine astrovirus (PAstV) has been studied in different parts and the virus has been found to be present in the Indian pig population. A study conducted in India from January 2013 to December 2017 reported a 17.6% prevalence of PAstV in diarrheic piglets (Kattoor et al., 2018). These findings indicate that PAstV is prevalent in pigs in India. The virus can cause diarrhea, vomiting, and even death in piglets, leading to economic losses in the pig industry, especially when present in mixed infections with other porcine pathogens. Study reported in Haryana state, India, found that 50% of the tested samples were positive for PAstV with co-infection of other enteric viruses (Vaishali et al., 2023). The co-infection of PAstV with other enteric viruses underscores the potential synergistic or interactive effects of multiple viral agents within the swine population. Such co-infections can have implications for disease severity, transmission dynamics, and overall health outcomes in affected pigs. Astroviruses are widely detected in multiple species with prevalence rates upto 10% and as high as 30% in humans in some developing countries. (De Grazia et al., 2011). With frequent discovery of novel astroviruses in both humans and animals, alongside advancements in genetic and evolutionary research, it has now become increasingly clear that astroviruses possess the ability to infect a diverse range of hosts across various environments. Moreover, their potential to cross barriers and adapt to new hosts is now well recognised.

Hepatitis E virus

Porcine Hepatitis E virus (HEV) is a single-stranded, positive sense RNA virus with a genome size of approximately 7.2 kilobases and belongs to the genus *Hepevirus* under the family *Hepeviridae*. The genome consists of three open reading frames (ORFs) and several non-coding regions. ORF 1 encodes for the non-structural polyprotein imperative for viral replication and transcription (Kumar et al., 2019). ORF 2 encodes capsid protein of virus and is major target for host immune responses, whereas ORF 3 codes for protein that modulates immune response of host and involved in virus egress (Machnowska et al., 2014). HEV isolates have been categorised into four closely related phylogenetic groups, or genotypes (Genotypes I-IV). These genotypes vary in terms of their geographical prevalence, the range of hosts they affect, and their infection patterns.

While its primary host is swine, the virus has garnered significant interest due to its ability to cross over to humans, highlighting its zoonotic potential and is an emerging public health concern in industrialised countries. Studies on people who work closely with pigs, like swine veterinarians and pig handlers, have discovered a higher occurrence of antibodies against HEV in these occupational groups which indicates a potential transmission of HEV from pigs to humans. The various possible transmission routes which lead to persistence of virus are depicted in Fig 1. Porcine HEV exhibits genetic resemblances to human HEV strains, making it an essential reservoir for potential zoonotic transmission. Genotype I and II are known to associated with humans and are large water-borne epidemics, circulating in Africa, Asia and Central America (Purcell et al., 2008). Genotype III causes sporadic outbreaks worldwide, responsible for infection in wild and domestic pigs and prevalent in United States, Europe, New Zealand, Thailand and Japan. Genotype IV is predominant in South East Asia and is widely prevalent in China, Japan, Indonesia, India and Vietnam (Li et al., 2022) conducted a global estimation of HEV prevalence in domestic pigs, wild boars, and pork products. The study revealed that approximately 60% of domestic pigs and 27% of wild boars have encountered HEV infection, as indicated by seroprevalence rates. Actively infected

animals, based on HEV RNA positivity, nearly 13% in domestic pigs and 9.5% in wild boars. Notably, about 10% of commercial pork products tested positive for HEV RNA, although data availability on this aspect is limited.

In developed countries, zoonotic transmission is considered the most prevalent pathway, but in India, it seems to be infrequent. In a study conducted by Vivek *et al.* (2011) in Vellore, India, they examined serum samples from 102 pigs and plasma from 34 swine handlers by RT-PCR and genotype of HEV. They observed HEV was detected in two pigs, and both viruses belonged to genotype 4. Interestingly, no HEV RNA was found in any of the swine handlers. However, 94.1% of swine handlers tested positive for antibodies against HEV. While the HEV genotype in swine differed from that in humans, the elevated antibody levels in swine handlers suggest a potential for zoonotic infections. This is evidenced by the substantial number of pigs in India having detectable anti-HEV antibodies, yet the virus isolates from them are predominantly GT4, distinct from those found in human cases. The epidemiology of HEV has not changed much over time in India (Aggarwal *et al.*, 2021). HEV diagnosis in pigs has been studied molecularly across various regions in India, encompassing the South (Vivek *et al.*, 2011), North and Northeast (Milton *et al.*, 2023).

Picobirnaviruses

Picobirnaviruses belong to the family *Picobirnaviridae* and are small, non-enveloped, double stranded RNA genomes consisting of the gene segment 1, larger segment (2.2 to 2.6 kbp) and gene segment 2, smaller segment (1.5 to 1.9 kbp) (Malik *et al.*, 2014). The genomic RNA of HEV consists of ORF 1 encoding viral non-structural proteins, ORF 2 encoding the putative capsid protein and ORF 3 encoding the cytoskeleton-associated phosphoprotein. The viral particle lacks an outer envelope and has a size ranging from 33 to 35 nm in diameter.

Porcine picobirnavirus has been detected in swine populations across different continents, indicating their widespread geographical distribution. It is responsible for causing diarrhea, whereas it has also been reported in the respiratory tract of pigs. Gaining insights into the geographic spread of virus is important to track their occurrence, genetic variation, and the potential threats they pose to both pig farming and humans. The zoonotic transmission of picobirna virus infection is suggested by the identification of genetically similar PBVs in both humans and animals. The genome reported from Hungary, Argentina, and Venezuela suggested that genogroup I of picobirna virus from pigs showed genetic similarity to human genogroup I picobirna virus. It has been widely reported in Asia including India (Kylla *et al.*, 2017), China, Sri Lanka, Hong Kong (Smits *et al.*, 2011), and Thailand (Wilburn *et al.*, 2017). It has been detected in several species from different countries, including in South America and different prevalence in different countries has been shown in Table 2.

Despite their minuscule size, picobirnaviruses have attracted significant attention due to their diverse genetic composition and interspecies transmission through genetic reassortment, mutation, and recombination leading to viral emergence (Reddy *et al.*, 2023).

Caliciviruses

The family *Caliciviridae* includes seven genera in mammals (Lagovirus, Norovirus, Nebovirus, Recovirus, Sapovirus, Valovirus, and Vesivirus) (Vinje *et al.*, 2019). Noroviruses and Sapoviruses are emerging enteric pathogens and members of the family *Caliciviridae* and cause widespread gastroenteritis and food-borne illness. Viruses in the family *Caliciviridae* are small, non-enveloped, positive-sense RNA genomes. The genome is approximately 7.4 to 8.3 kb in length, and encode for various viral proteins that are essential for the replication and pathogenicity of the virus.

Norovirus is associated with diarrhea and gastrointestinal disease in swine and is transmitted via fecal-oral route. The wide host range of norovirus and their ability to cross-species transmission leads to the possibility of zoonotic transmission. While the prevalence and distribution may vary from region and over time, the virus has been reported in countries including Canada, the United States, Japan, Italy, China, and South Africa (Scheuer *et al.*, 2013; Nakamura *et al.*, 2016; Di Bartolo *et al.*, 2014) with varying prevalence as shown in Table 2.

Sapoviruses are emerging as an important zoonotic pathogen responsible for causing gastroenteritis in animals and humans. The virus primarily causes gastroenteritis, causing symptoms like diarrhea, vomiting, and dehydration. Out of the eight defined genogroups of sapovirus (GI-IX), three genogroups (GIII, GV, and GVI) have been identified for porcine sapovirus (Nagai *et al.*, 2020). Porcine sapovirus is reported in faeces of asymptomatic pigs, diarrheic pigs with co-infections with other pathogens (Dufkova *et al.*, 2013; Scheuer *et al.*, 2013). Sapovirus is widely prevalent in Denmark, Finland, Hungary, Italy, Slovenia, Spain, Ireland, Japan, Korea, Slovakia, United States, Brazil, and China (Shen *et al.*, 2011; Scheuer *et al.*, 2013; Salamunova *et al.*, 2018) with varying prevalence as shown in Table 2.

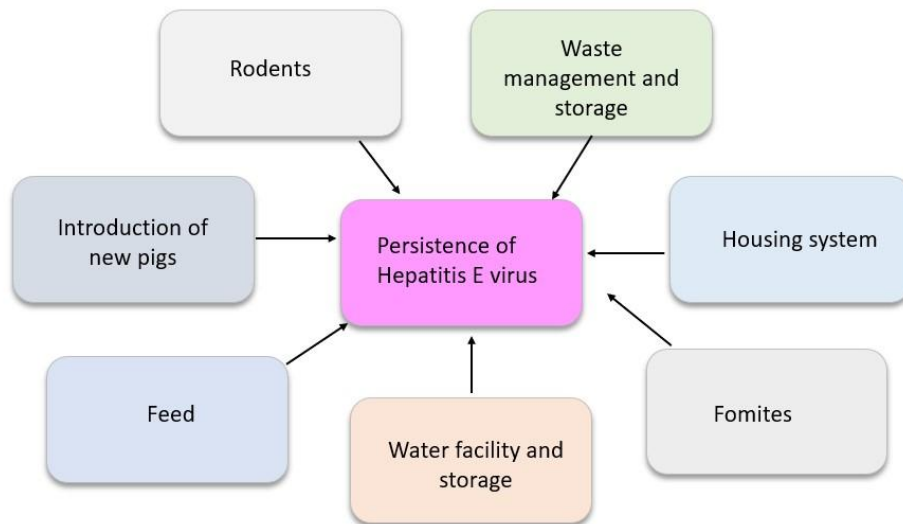
Porcine calicivirus is not typically associated with genetic risks in the way that human predispositions are related to certain diseases. The genetic variability of porcine calicivirus can affect the risk of infection (Aniță and Aniță, 2022). Different strains can have varying levels of pathogenicity. It is crucial to emphasize that there are no identified inherent genetic factors in pigs that render them either more susceptible or less resistant to porcine calicivirus.

Table 1. Prevalence of porcine rotavirus A in different nations by different diagnostic approaches.

	Samples collected	Year	Country	Detection method	Prevalence	References
North America	Fecal samples	2004, 2001-2012	Ohio	RT-PCR	9.4% (35/371)	Amimo et al., 2013
South America	Oral fluids and fecal samples	2015-2018	Chile	Real time RT-PCR	38% (58/154)	Neira et al., 2023
Africa	Fecal samples	2016	Mozambique	ELISA	11.8% (34/288)	Boene et al., 2021
Europe	Stool specimens	2018-2019	Spain	RT-PCR	44.9% (389/886)	Monteagudo et al., 2022
Asia	Diarrheic piglet feces	2017-2019	China	RT-PCR	16.83% (100/594)	Tao et al., 2023
	Fecal samples	Nov 2016- March 2017 & Dec 2017- March 2018	India	RNA-PAGE and RT-PCR	7.94% (17/214) & 10.28% (22/214)	Abass et al., 2022

Table 2. Identification of different porcine viruses in various countries using RT-PCR

Samples	Year	Country	Prevalence	References
Fecal samples	Nov 2011 - June 2012	China	20.9% (39/187)	Smits et al., 2011
Fecal samples	June 2013 - May 2015	India	11.15% (51/457)	Kylla et al., 2017
Fecal samples	Jan 2014 - Feb 2015	Thailand	29.4% (112/380)	Wilburn et al., 2017
Fecal samples	2018	Japan	5.8% (11/190)	Nakamura et al., 2016
Fecal samples	March - June 2017	Italy	2.53% (2/79)	Di Bartolo et al., 2014
Fecal samples	July 2022 - March 2023	Vietnam	4.9% (5/102)	Van Dong et al., 2024
Stool samples	April 2008 - March 2009	China	0.9% (8/904)	Shen et al., 2011
Rectal swabs	2013-2016	Slovakia	9% (37/411)	Salamunova et al., 2018
Fecal swab	2019	Korea	3% (9/296)	Lyoo et al., 2020
Fecal samples	July 2022 - March 2023	Vietnam	9.8% (10/102)	Dong et al., 2023


Fig. 1: Various routes of transmission of Hepatitis E virus.

Conclusion

Porcine enteric viruses have zoonotic potential with inter species transmission leading to heavy economic losses. The key to controlling and preventing the virus's transmission within swine populations lies in effectively managing and mitigating environmental risk factors, implementing rigorous biosecurity measures, and upholding high standards of animal husbandry practices. Continued surveillance of porcine enteric viruses is needed to define their zoonotic potential, epidemiology and public and animal health impact.

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