Zoonotic and Reverse Zoonotic Transmission of SARS-CoV-2 Virus: A Perspective on Human-animal Interface

22

Aziz Ul-Rahman[1*], Muhammad Abu Bakr Sbabbir[2], Majeeda Rasheed[3], Naheed Bano[1], Muhammad Furqan Shahid[4], Momena Habib[5], Rauf Mehmood[6], Nusrat Shafi[7], Hafeez Ur Rehman Ali Khera[1], Samar Wafa Kabeer[1], Kalsoom Abdul Razaq[1], Junaid Ali Khan[1] and Muhammad Asif Raza[1,8]

ABSTRACT

The emergence of SARS-CoV-2 has underscored the crucial interaction between humans and animals, offering a unique perspective on the dynamics of zoonotic and reverse zoonotic transmission. This chapter aims to consolidate current knowledge on the two-way transmission of SARS-CoV-2 across the human-animal interface. We delve into the zoonotic origins of the virus, exploring potential reservoir hosts and intermediary species. Additionally, we summarize various events of reverse zoonosis, where humans have transmitted the virus to animals, raising concerns about the establishment of viral reservoirs in diverse species. This bidirectional transmission has significant implications for public health, necessitating a holistic approach to disease surveillance, wildlife conservation, and one health strategies. The evidence of zoonosis and reverse zoonosis sheds light on the expansive spectrum of potential hosts susceptible to SARS-CoV-2 infection, emphasizing the dynamic interplay within the host landscape. These phenomena not only underscore the intricate host dynamics of the virus but also emphasize the ability of various species to act as reservoirs, transmitters, or carriers, potentially contributing to pandemics among humans. By comprehensively understanding the intricacies of SARS-CoV-2 transmission dynamics at the human-animal interface, we can enhance our preparedness to mitigate future zoonotic events and safeguard both human and animal health.

Keywords: SARS-CoV-2, Zoonosis, Reverse zoonosis, Human-animal interface, Host dynamics

CITATION

Ul-Rahman A, Sbabbir MAB, Rasheed M, Bano N, Shahid MF, Habib M, Mehmood R, Shafi N, Khera HURA, Kabeer SW, Razaq KA, Khan JA and Raza MA, 2023. Zoonotic and reverse zoonotic transmission of SARS-CoV-2 virus: A perspective on human-animal interface. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 269-282. https://doi.org/10.47278/book.zoon/2023.102

CHAPTER HISTORY Received: 15-Jan-2023 Revised: 27-March-2023 Accepted: 18-Aug-2023

[1]Faculty of Veterinary and Animal Sciences, MNS University of Agriculture, Multan 66000, Pakistan
[2]Institute of Microbiology, University of Veterinary and Animal Sciences, Lahore 54000, Pakistan
[3]Department of Life Sciences, Khawaja Fareed University of Engineering and Information Technology (KFUEIT), Rahim Yar Khan 64200, Pakistan

[4]Veterinary Research Institute, Department of Livestock and Dairy Development, Government of Punjab, Zarar Shaheed Road Lahore 54000 Pakistan
[5]Department of Microbiology and Molecular Genetics, University of Okara, Okara 56150, Pakistan
[6]Quality Control Department, Assir Cooperative Company, Muhayil Assir 61913, Kingdom of Saudi Arabia
[7]Chaudhary Pervaiz Elahi Institute of Cardiology, Multan 66000, Pakistan
[8]Deparment of Animal Sciences, Faculty of Animal and Agricultural Sciences, Universitas Diponegoro, Semarang 20275, Central Java Indonesia
***Corresponding author:** drazizangel@gmail.com

1. INTRODUCTION

Zoonotic pathogens, originating from wildlife, have a significant impact on both public and animal health leading to epidemics and pandemics (Bengis et al. 2004). The emergence and re-emergence of viral pathogens have resulted in a global burden of infectious diseases, billions of cases and millions of fatalities. Before becoming a zoonotic pathogen, a virus of wildlife origin must overcome various hurdles, including ecological, behavioral, interspecies and immunological barriers (Plowright et al. 2017). Some animals can act as epidemiological bridges and serve as intermediate hosts in transmitting viruses from animals to humans.

Practices like intensive animal husbandry, close contact between animals and humans, and urbanization can create opportunities for the spillover of zoonotic viruses at the human-livestock interface (Magouras et al. 2020). Conversely, humans in close contact can also transmit viruses to animals, particularly domestic and companion animals, leading to reverse zoonosis (Messenger et al. 2014). These zoonotic and reverse zoonotic events raise concerns about infected hosts becoming ill, shedding viruses into the environment, and potentially reintroducing viruses among susceptible hosts (Goraichuk et al. 2021).

Recently, a novel respiratory illness known as COVID-19 appeared in China, in late 2019 and become a major global health challenge. This pandemic occurred due to infection in humans with SARS-CoV-2. Following previous outbreaks of other coronaviruses, the SARS-CoV-2 virus is more contagious and poses a significant threat to human health with substantial economic losses (Adil et al. 2021). Initially, the origin and spread of this virus was a subject of controversy and therefore, numerous studies have investigated its zoonotic potential by examining its ability to infect various animal species (Sit et al. 2020; Bessière et al. 2021; Gortazar et al. 2021; Grome et al. 2022; Purves et al. 2023). Conversely, the virus has also shown the ability to transmit from humans to animals, resulting in varying degrees of infection in different animals. The capability of zoonosis and reverse zoonosis of this virus poses serious threats to animal and public health (Kumar et al. 2020; Olival et al. 2020; Dróżdż et al. 2021; Fischhoff et al. 2021). Despite detailed reports, information on the transmission of the SARS-CoV-2 virus (Fig. 1), particularly focusing on a wide range of susceptible hosts and the propensity for inter and cross-species transmission is scattered. Understanding its transmission is crucial in linking all susceptible hosts and comprehending the larger evolutionary dynamics to develop effective disease control strategies and diagnostic approaches. Therefore, this chapter aims to compile scattered information on zoonotic and reverse zoonotic infections or transmission events of the SARS-CoV-2 virus and draw the global scientific community's attention to its public health concerns.

2. ZOONOTIC ORIGIN AND TRANSMISSION

The SARS-CoV-2 virus is a member of the *Coronavirus* genus within the family *Coronaviridae*, which comprises seven different viruses with the potential to cause zoonotic infections in humans (Hu et al.

2021). The CoVs typically target the respiratory system and cause flu-like infection in humans and have been identified in various animals, including birds, rodents, and domestic animals. Comparative studies suggest that all CoVs likely originated from bats, mice, and cattle before being transmitted to humans (Segars et al. 2020; Dróżdż et al. 2021). Other CoVs are believed to be originated from bats and caused outbreaks in humans through various intermediate hosts including civets and camel. Likewise, the COVID-19 pandemic is believed to have emerged from zoonotic transmission, with the SARS-CoV-2 virus likely to originate in animals before being transmitted to humans (Dróżdż et al. 2021). While the exact origin is still under investigation, bats are widely considered the likely source, with a potential intermediate host involved in the transmission to humans, possibly a pangolin, based on genetic similarities (Ul-Rahman et al. 2020).

Various bat species may harbour a diverse range of CoVs, and their close interaction with humans in certain regions may have facilitated spillover events (Banerjee et al. 2021). The immune system of bats has garnered significant scientific interest due to its potential implications for human health. Bats' ability to control viral infections effectively while minimizing harmful inflammatory responses has drawn attention as it could provide valuable insights into developing strategies for managing viral diseases in humans. By studying the molecular and genetic mechanisms underlying bats' immune adaptations, researchers aim to investigate various interventions and preventive approaches to reduce the impact of viral infections and transmission to humans. Bats may serve as natural models for investigating host-virus interactions and may hold the key to innovative approaches for combating viral diseases in humans (Letko et al. 2020).

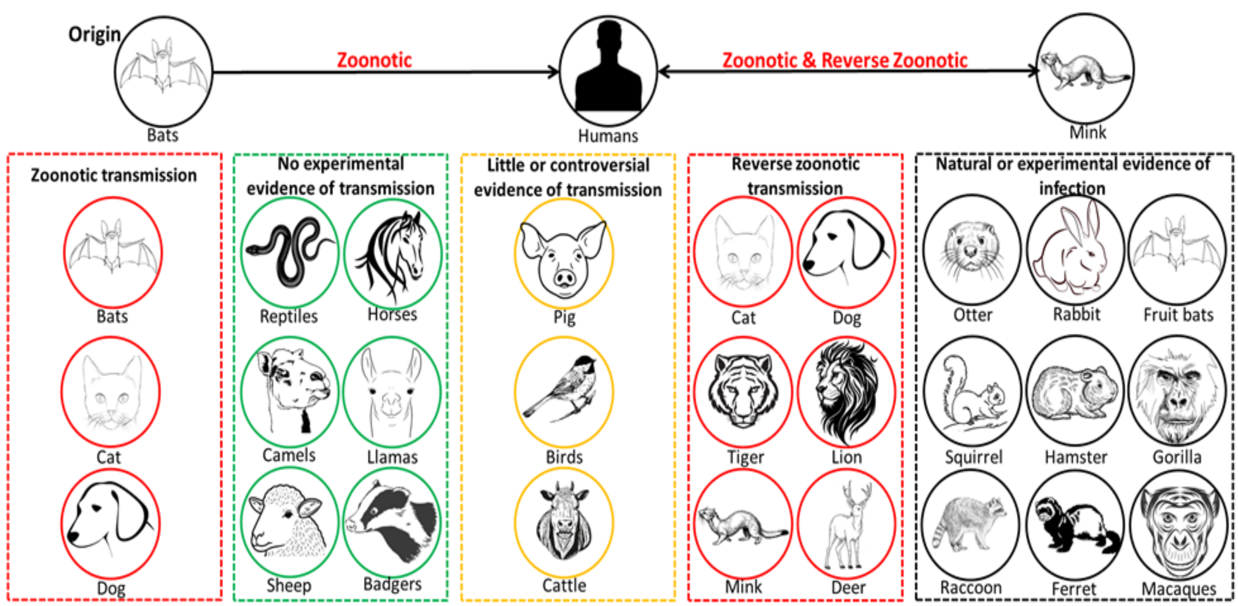

Fig. 1: Susceptibility of a wide range of domestic and wild animals to natural or experimental infection of SARS-CoV-2 virus across the globe.

The spread of the SARS-CoV-2 virus among human and animal populations can occur through diverse mechanisms, which include both direct and indirect routes. Individuals who have close contact with infected bats or handle infected wildlife are at higher risk of contracting zoonotic infections due to the initial spillover of the virus. Additionally, the virus can be spread via respiratory droplets, aerosols, contact with contaminated surfaces, and the consumption of infected animal products (Zhou and Shi

2021). Previous studies have suggested that numerous animals can act as intermediate hosts for the transmission of viruses at animal-to-human, animal-to-animal, human-to-human, and human-to-animal interfaces (Hedman et al. 2021; Brüssow 2023). However, the identification of intermediate hosts that facilitate the transmission of the SARS-CoV-2 virus between susceptible hosts remains an active area of scientific investigation and is still debatable.

3. CROSS- AND INTER-SPECIES TRANSMISSION

The potential of the SARS-CoV-2 virus to transmit between various animals has become a major cause of concern, as it raises significant questions about the virus's infectivity and spread across various hosts. The potential of a virus being transmitted across species barriers is a complex process that is influenced by various factors, including viral attachment, adaptation, and molecular interactions (Dhama et al. 2020). For most viruses, such as the influenza virus and SARS-CoV-2 virus, interactions between donor and recipient hosts play a crucial role in facilitating the transmission to overcome cross species barriers. The behaviour and activities of hosts in shared geography or habitats can play a significant role in either facilitating or hindering virus transmission among a wide range of susceptible hosts. Human activities, particularly those that promote close contact between infected hosts and uninfected hosts, can increase the risk of zoonosis and reverse zoonosis (Ayim-Akonor et al. 2020; Goraichuk et al. 2021).

Numerous cases of species-to-species transmission of the SARS-CoV-2 virus has been documented, offering valuable insights into its adaptability and ability to infect different animal species (Abdel-Moneim and Abdelwhab 2020; Leroy et al. 2020; Salajegheh Tazerji et al. 2020; Oude Munnink et al. 2021). Previous studies also confirmed that the virus has been found to spread rapidly among the mink population and found evidence of human-to-mink transmission and mink-to-human transmission, indicating the bidirectional nature of cross-species transmission (Fenollar et al. 2021; Hammer et al. 2021; Lu et al. 2021; Oude Munnink et al. 2021). The occurrence of transmission within a recipient population depends on intraspecific contacts that play a crucial role in the transmission of the virus. The ability of the virus to cause infection or remain persistent in various hosts is dependent on factors such as population density, mixing patterns between donor and recipient host species, and biological phenomena against a pathogen (Lim et al. 2016). Previous serological studies highlighted that domestic cats residing in proximity to mink farm had specific antibodies for the SARS-CoV-2 virus, suggesting both zoonotic and animal-to-animal transmission (Zhang et al. 2020; Barua et al. 2021; Udom et al. 2022). Airborne transmission of the SARS-CoV-2 virus has also been reported between cats and hamsters (Yen et al. 2022). Additionally, natural infection of the SARS-CoV-2 virus has been reported in captive/domestic ferrets (Giner et al. 2021).

Considering transmissibility, virulence, and the degree of infection in various hosts, the World Organization for Animal Health (WOAH) recognizes the potential implications of such events for public health and the effectiveness of treatment and vaccines. It's worth noting that few hosts, including domestic and companion pets, can develop an infection with or without showing clinical signs and potentially lead to zoonotic and reverse zoonotic transmission by shedding the virus into the environment. Individuals directly associated with animal welfare management, including zoo workers, farmers, veterinarians, and animal lovers, are at high risk of zoonotic infections (EFSA 2023). Moreover, intermediate hosts can play a critical role in inter- and cross-species transmission of the SARS-CoV-2 virus by serving as a bridge between the original reservoir species and the target host species. These intermediate hosts may provide an environment conducive to viral replication and transmission, allowing the virus to adapt to new cellular and immune systems (Zhao et al. 2020). Identifying and studying these intermediate hosts is crucial for understanding the dynamics of inter- and cross-species transmission and implementing preventive measures.

4. MOLECULAR MECHANISM OF CROSS-SPECIES TRANSMISSION

Various biological factors play a crucial role in the ability of a virus to switch species and facilitate cross-species transmission. One important factor is the expression of receptors during cell attachment, which can increase the virus's capability to infect a new host. After virus attachment to the host cell, viral protein, and cellular machinery play a vital role in virus replication and dissemination to another host (Kane et al. 2023). A virus that can replicate at a high level within a host is generally more capable of being transmitted to other hosts. In case of SARS-CoV-2 virus, it has been observed to replicate efficiently in cats and ferrets, leading to transmission to other species. However, the limited replication of the virus in dogs, chickens, and pigs suggest restricted transmission in these species (Hossain et al. 2021). The molecular mechanism by which the SARS-CoV-2 virus targets different species involves the interaction between viral proteins, particularly the spike protein, and cellular receptors on host cells. The spike protein plays a pivotal role in facilitating virus attachment to host cells and determining the host range and tropism of the virus. The primary receptor for SARS-CoV-2 is ACE2 which is present in various human tissues. However, the expression and availability of ACE2 receptors in a wide range of animals can vary and influence host susceptibility to infection (Luan et al. 2020).

The capability of SARS-CoV-2 to infect different species is usually influenced by the presence and structure of ACE2 receptors in the target species. Some animal species may have ACE2 receptors with a higher affinity for the viral spike protein, facilitating efficient viral entry and replication. The spike protein, particularly the receptor-binding domain, plays a crucial role in infecting various hosts by binding to ACE2 receptors (Liu et al. 2021). To successfully infect a new host species, the receptor-binding domain may undergo genetic mutations that enable it to interact with ACE2 receptors in the target species. These genetic mutations may facilitate the attachment potential of the spike protein and host receptor, enhancing the viral entry mechanism into cells of new host species (Liu et al. 2021). Apart from the receptor-binding domain and its interaction with cellular receptors, other cellular factors and host immune responses, including innate and adaptive immune mechanisms, can influence the potential of the virus to infect and replicate in different species (Liu et al. 2021).

5. ZOONOTIC AND REVERSE ZOONOTIC EVENTS IN PET ANIMALS

Distinct coronaviruses of animals, domestic cats and dogs are now considered to have an infection by acquiring and shedding the SARS-CoV-2 virus into the environment (Bosco-Lauth et al. 2020; Patterson et al. 2020). Since the start of the pandemic, sporadic cases of cross- and intra-species transmission of the SARS-CoV-2 virus in domestic cats have been reported from various countries (Table 1). Various experimental studies have highlighted the susceptibility of cats to get infection and spread the virus to other pets and humans through respiratory droplets (Bosco-Lauth et al. 2020; Bao et al. 2021; Decaro et al. 2021). The detection of neutralizing antibodies also indicated the natural infection in cats in China (Deng et al. 2020). Similarly, previous studies observed the existence of anti-SARS-CoV-2 antibodies in domestic cats in Italy and France, where the owner or family members suspected or confirmed COVID-19 cases (Fritz et al. 2020; Patterson et al. 2020).

Notably, a study reported an active infection in cats having a clinical presentation of COVID-19 which was residing in the vicinity of mink farms facing outbreaks (Amman et al. 2022; van Aart et al. 2022). Despite evidence of active infection, the route of spread or source of infection in cats remains uncertain and unclear. Emerging evidence emphasizes that cats may develop non-sterilizing immunity following natural infection and remains susceptible to reinfection to spread disease into the human and cat population. On the other hand, evidence on human-to-cat transmission following the identification of active COVID-19 cases in cat owners in Belgium and Hong Kong highlighted the reverse zoonosis (Barrs et al. 2020; Garigliany et al. 2020). The genome of the virus was detected in cat vomit, faeces, and nasopharyngeal

and rectal swabs in France. The substantial evolutionary analysis highlighted that the isolated SARS-CoV-2 strains originating from cats belonged to a phylogenetic clade that was predominant among French human clinical cases (Sailleau et al. 2020). Similarly, cats from a household in Spain exhibited SARS-CoV-2 infection and were found positive through oropharyngeal swab testing (Segalés et al. 2020).
Experimental studies have indicated that infected dogs typically shed minimal to no virus, suggesting a low risk of contracting and transmitting the virus (AVMA 2020; Van Aart et al. 2022). However, there have been isolated cases of dogs testing positive for SARS-CoV-2 in various countries (Table 1). In these cases, the SARS-CoV-2 virus genome was found in samples collected from dogs having no clinical presentation of COVID-19 infection. On the other hand, numerous studies conducted in American and European countries observed a varying clinical presentation of COVID-19 infection in dogs (AVMA 2020; Sit et al. 2020; Van Aart et al. 2022). However, there is still some disagreement regarding the presence of the virus and its transmission to humans from dogs. Several studies have noted a higher risk of dogs being exposed in households with confirmed COVID-19 cases (Bosco-Lauth et al. 2020; Sit et al. 2020; Decaro et al. 2021). However, definitive evidence of transmission between pets and humans is currently lacking. As a precautionary step, it is advisable to include pets in self-isolation measures. These findings underscore the importance of further research to understand how domestic pets contract the virus and transmit it to other animals or humans.

6. SUSCEPTIBILITY OF MINKS, FERRETS, RABBITS AND PANGOLIN

Mink farms have been at the center of outbreaks due to the ability to transmit the virus from humans to minks and leading to widespread infections among the mink population (Oreshkova et al. 2020; Aguiló-Gisbert et al. 2021; Domańska-Blicharz et al. 2021; Fenollar et al. 2021; Hammer et al. 2021).
These outbreaks have been reported in several American and European countries. It is speculated that the outbreaks among the mink population were associated with active COVID-19 cases of farmers and/or staff members or their family members and the similarity index between SARS-CoV-2 sequences isolated from humans and minks confirmed the transmission from mink to humans (Fenollar et al. 2021). These reports prompted a thorough investigation to understand the potential routes of transmission and assess the associated environmental and occupational hazards, including the risk of transmission from infected mink to humans. The transmission of SARS-CoV-2 to farmed mink has had devastating effects, leading to increased mortality rates and significant economic losses in mink farming. The introduction of the virus in mink farms occurred through infected farm workers who had close contact with the animals (Oude Munnink et al. 2021).
Once the virus was introduced, it spread rapidly among the minks, resulting in a high number of infected animals. To control the outbreaks and prevent further transmission, infected minks on affected farms were euthanized, and strict testing measures were implemented to monitor the situation. During these outbreaks, genetic changes were observed in the virus as it circulated within the mink population. This indicates that the virus can undergo genetic modifications during transmission among minks (Ren et al. 2021). These genetic changes raise concerns about the potential for the virus to evolve and adapt within animal populations, which could have implications for public health and the effectiveness of vaccines and treatments. The researchers found that the viral strain detected in the minks was found to be identical to the strain circulating in humans in Denmark and emphasized the circulation of the same virus strains (Oude Munnink et al. 2021). Furthermore, a pet ferret residing in a household with a confirmed COVID-19 patient case also tested positive for the virus (Račnik et al. 2021).
Thus, it is speculated that minks and ferrets are involved in the transmission of the SARS-CoV-2 virus among human and other animal populations. Initially, there was speculation that pangolins, particularly the Malayan pangolin (*Manis javanica*), may play a pivotal role as intermediate hosts in transmitting the

Table 1: Zoonotic and reverse zoonotic events related to natural and experimental infection of SARS-CoV-2 in a wide range of domestic and wild animals

Host species	Infection	Transmission	Country	References
Cat	Natural	Cat-to-cat	China	Bao et al. 2021
	Natural	Cat-to-human	USA, Netherland, Hong Kong	AVMA 2020
	Natural	Cat-to-cat, cat-to-human	France	Bessière et al. 2021
	Natural	Human-to-cat	Greece, Cyprus, UK, Switzerland, Germany, Chile, Italy	Michelitsch et al. 2020; Chaintoutis et al. 2021; Curukoglu et al. 2021; Hosie et al. 2021; Klaus et al. 2021; Neira et al. 2021; Pagani et al. 2021; Zoccola et al. 2021
	Experimental	Cat-to-cat	USA, Germany	Gaudreault et al. 2022a; Halfmann et al. 2020; Braun et al. 2021
Dog	Natural	Human-to-dog	Hong Kong	Sit et al. 2020
	Natural	Dog-to-human	USA, Spain, Russia, France, Germany	AVMA 2020
Cattle	Experimental	No intraspecies transmission	Germany	Ulrich 2020
Poultry and avian species	Experimental	No intraspecies transmission	China, USA	Shi et al. 2020; Suarez et al. 2020
Pig	Experimental	None	China	Shi et al. 2020
Rabbit	Experimental	None	New Zealand	Mykytyn et al. 2021
Domestic Ferret	Natural	Human-to-ferret	Spain	Gortazar et al. 2021
Syrian Golden Hamster	Experimental	Hamster-to-hamster	China	Chan et al. 2020
Mink	Natural	Human-to-mink, Mink-to-mink, Mink-to-human	Netherland	Oreshkova et al. 2020; Van Aart et al. 2022
Rodents including mouse, wood rat, raccoon, and squirrel	Experimental	No intraspecies transmission	USA	Bosco-Lauth et al. 2021
Otters	Natural	Not reported	USA	APHIS 2021a
Fruit Bats	Experimental	Bat-to-bat	Germany	Schlottau et al. 2020
Tiger	Natural	Human-to-Tiger, Tiger-to-tiger	USA	Grome et al. 2022
Lion	Natural	Human-to-Lion, Tiger-to-Lion, Lion-to-Lion	USA	McAloose et al. 2020
Rhesus Macaques	Experimental	Intraspecies transmission	China, USA	Deng et al. 2020; Munster et al. 2020
Western Lowland Gorilla	Natural	intraspecies transmission	USA	APHIS 2021b
White-Tailed Deer	Natural and experimental	Perinatal transmission, intraspecies transmission	USA	Cool et al. 2022
Fallow Deer	Natural and experimental	Human-wildlife transmission	USA	Purves et al. 2023

SARS-CoV-2 virus. This was due to the discovery and evolutionary trend of SARS-CoV-2-like coronaviruses in confiscated pangolins, as well as the identification of pangolin cell types that might be susceptible to the virus (Liu et al. 2020; Ul-Rahman et al. 2020). The potential role of rabbits as hosts of SARS-CoV-2 has also been examined, considering their farming for meat and fur (Mykytyn et al. 2021). In a study involving young New Zealand white rabbits, the animals were intentionally infected with the virus and monitored for 21 days. Despite the absence of clinical signs of infection, the rabbits were found to shed the virus in nasal and oropharyngeal secretions and exhibited evidence of seroconversion (Pomorska-Mól et al. 2021; Fritz et al. 2022). Notably, the study's findings may not be representative of infections in rabbits of different ages or breeds, highlighting the need for further research on the potential of rabbits as hosts of the virus. The susceptibility of mink, ferrets, and rabbits to SARS-CoV-2 infection highlights the importance of implementing strict biosecurity measures in animal farming environments to prevent the transmission of viruses from humans to animals and vice versa. Continued surveillance and monitoring of both human and animal populations are crucial to better understand and mitigate the risks associated with reverse zoonotic transmission.

7. SUSCEPTIBILITY OF LIVESTOCK AND WILD ANIMALS

The potential of virus transmission among animals and humans is now considered a serious concern because of the establishment of carriers or reservoirs, especially in regions with frequent human-animal contact and high livestock density. Recently, researchers intentionally infected six cattle with the virus, but found no transmission to other animals residing in close proximity (Ulrich 2020; Bosco-Lauth et al. 2021). Despite the absence of natural transmission, a study claimed a low level of viral shedding from infected cattle into the environment (Ulrich 2020). Similarly, the SARS-CoV-2 virus does not have the potential to infect livestock species, including sheep, camels, and llamas (Bosco-Lauth et al. 2021; Chouchane et al. 2021; Xu et al. 2021; Gaudreault et al. 2022b; Hong et al. 2022). However, previous studies claimed the susceptibility of various wild animals to SARS-CoV-2 infection (Table 1).
After the first case of SARS-CoV-2 infection in Malayan tigers, other tigers, and lions residing at the same zoo were also found to be infected in a Zoo in New York. It is noteworthy that the SARS-CoV-2 sequence isolated from infected tigers was found to have the highest genomic identity with sequences isolated from zoo keepers and clinical cases reported from the same city. However, the substantial analysis of the whole-genome sequences of the SARS-CoV-2 virus highlighted that lions and tigers were affected by distinct SARS-CoV-2 strains and indicated separate transmission events (McAloose et al. 2020). Through genetic and epidemiological analysis, it was determined that transmission from humans to tigers had occurred, specifically from zookeepers. However, the source of infection for the lions remained unclear. This indicated that the infection was likely transmitted from an asymptomatic zookeeper to the tigers (Bartlett et al. 2021). Wild animals exhibited varying SARS-CoV-2 infections showing asymptomatic infection to different clinical presentations. In all cases, staff members at the zoo also found positive for COVID-19, indicating possible transmission of the SARS-CoV-2 virus between humans and wild animals (McAloose et al. 2020; Grome et al. 2022).

8. EXPERIMENTAL INFECTION IN VARIOUS HOSTS

During the COVID-19 pandemic, there is a growing need to identify suitable animal models for studying the pathology of the disease and evaluating potential therapeutics and vaccines. Experimental infections have been conducted to study the susceptibility and transmission potential of SARS-CoV-2 in various wild animal species and provide crucial insight into the susceptibility of a wide range of hosts (Table 1). These studies showed that a large number of animals including rodents are highly susceptible to infection and can play a vital role in the shedding of virus into the environment and subsequent transmission to other animals (Abdel-Moneim and Abdelwhab 2020; Sun et al. 2020).

In the experimental studies, it is observed that the virus can effortlessly replicate in the respiratory and gastrointestinal tract of various animals and elicit immune responses for the synthesis of neutralizing antibodies. Upon re-infection, it was noted that cats cannot shed an adequate virus into the environment that is required for transmission to other cats (Gaudreault et al. 2022a). Similarly, cattle, dogs, and domestic pigs have shown poor viral replication while poultry species are not susceptible to the virus (Meekins et al. 2020; Schlottau et al. 2020). Among rodents, hamsters and ferrets showed susceptibility to acquiring SARS-CoV-2 infection and the ability to shed the virus for further transmission to susceptible hosts. Several non-human primates showed susceptibility to acquiring SARS-CoV-2 infection and have shown clinical presentations similar to those observed in COVID-19 patients. Due to viral replication and severe infection of the SARS-CoV-2 virus, non-human primates are now commonly used as models for biomedical research (Gonçalves et al. 2021).

9. POTENTIAL OF MECHANICAL TRANSMISSION

Arthropods can pose challenges by acting as potential vectors for pathogens that can be transmitted to humans and other animals. Arthropods or pests including rats, mosquitoes, mice, houseflies, ticks, and cockroaches are usually prevalent in various environments, including public places, farms, and healthcare settings (Nekoei et al. 2022). These pests can come into contact with contaminated surfaces, potentially acquiring and transmitting pathogens. Previous research has indicated that arthropods, including ticks, houseflies, mosquitoes, and midge can mechanically transmit the virus (Reuben et al. 2020; Balaraman et al. 2021 a,b). Recent experimental studies demonstrated that houseflies can spread the virus into the environment for up to 24 hours following exposure to the virus (Montes et al. 2020; Balaraman et al. 2021a). Previous studies have shown that houseflies can acquire and carry infectious viral particles for a short period of time after exposure. They can retain the virus in their bodies for up to 24 hours, suggesting the potential for mechanical transmission (Balaraman et al. 2021a). This finding highlights the potential role of houseflies in the transmission and dissemination of the virus, raising concerns about the importance of implementing measures to control insect vectors and prevent further spread of COVID-19. According to recent research, there is evidence suggesting that biting midges and mosquitoes do not facilitate the replication of SARS-CoV-2 and are improbable to act as biological vectors for the virus (Balaraman et al. 2021b).

Passive or mechanical transmission occurs when pests carry the virus on their body parts or mouthparts and transfer it to other hosts, without virus replication or development within the pests themselves (Reuben et al. 2020). Studies have shown that the virus does not replicate in Aedes mosquito cells, and live Aedes mosquitoes collected during the pandemic showed no signs of carrying the virus. Furthermore, injecting mosquitoes with the virus did not result in any viral replication (Huang et al. 2020; Xia et al. 2020). Similarly, experiment with biting midges and certain Culex mosquito species also indicated that they do not support viral replication when feeding on infected blood (Reuben et al. 2020).

10. CONCLUSION

The COVID-19 pandemic has had a profound impact on human lives, the economy, and daily routines. This disease, believed to have originated in bats, has brought attention to the potential for zoonotic transmission, where diseases pass from animals to humans. However, we must also consider the possibility of reverse zoonosis, where the virus can be transmitted from humans back to animals. Cases of SARS-CoV-2 infections have been documented in various animal species, including pets, zoo animals, and certain farm animals. These findings hold significant importance in comprehending the possible involvement of various animal species in the transmission and dissemination of SARS-CoV-2. Moreover, they aid in formulating appropriate control strategies to manage the spread of the virus effectively. To reduce the risk of zoonotic and reverse zoonotic events, it is crucial to incorporate vulnerable animals into surveillance strategies. This includes monitoring pets, farm, zoo and laboratory animals, and animals used in biotechnology production. By embracing the One Health approach, interdisciplinary collaboration among professionals in human and animal health, environmental science, policymaking, and other relevant fields can protect the health of humans, animals, and the environment, ultimately mitigating the risks of future pandemics.

REFERENCES

Abdel-Moneim AS and Abdelwhab EM, 2020. Evidence for SARS-CoV-2 infection of animal hosts. Pathogens 9(7): 529.

Adil MT et al., 2021. SARS-CoV-2 and the pandemic of COVID-19. Postgraduate Medical Journal 97(1144): 110-6.

Aguiló-Gisbert J et al., 2021. First description of SARS-CoV-2 infection in two feral American mink (Neovison vison) caught in the wild. Animals 11(5): 1422.

Amman BR et al., 2022. GPS Tracking of Free-Roaming Cats (Felis catus) on SARS-CoV-2-Infected Mink Farms in Utah. Viruses 14(10): 2131.

APHIS, Animal and Plant Health Inspection Service, U.S. Department of Agriculture. Confirmation of COVID-19 in Gorillas at a California Zoo, 2021a. Available online: https://www.aphis.usda.gov/aphis/newsroom/stakeholderinfo/sa_by_date/sa-2021/sa-01/ca-gorillas-sars-cov-2

APHIS, Animal and Plant Health Inspection Service, U.S. Department of Agriculture. Confirmation of COVID-19 in Otters at an Aquarium in Georgia, 2021b. Available online: https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa_by_date/sa-2021/sa-04/covid-georgia-otters

AVMA, 2020. In-depth summary of reports of naturally acquired SARS-CoV-2 infections in domestic animals and farmed or captive wildlife. Available from:https://www.avma.org/resources-tools/animal-healthand-welfare/covid-19/depth-summary-reportsnaturally-acquired-sars-cov-2-infections-domesticanimals-and-farmed-or.

Ayim-Akonor M et al., 2020. Exposure of domestic swine to influenza A viruses in Ghana suggests unidirectional, reverse zoonotic transmission at the human–animal interface. Zoonoses and Public Health 67(6): 697-707.

Balaraman V et al., 2021a. Mechanical transmission of SARS-CoV-2 by house flies. Parasites and Vector 14: 1-9.

Balaraman V et al., 2021b. Susceptibility of midge and mosquito vectors to SARS-CoV-2. Journal of Medical Entomology 58(4): 1948-51.

Banerjee A et al., 2021. Unraveling the zoonotic origin and transmission of SARS-CoV-2. Trends in Ecology and Evolution 36(3): 180-4.

Bao L et al., 2021. Susceptibility and attenuated transmissibility of SARS-CoV-2 in domestic cats. The Journal of Infectious Diseases 223(8): 1313-21.

Barrs VR et al., 2020. SARS-CoV-2 in quarantined domestic cats from COVID-19 households or close contacts, Hong Kong, China. Emerging Infectious Diseases 26(12): 3071.

Bartlett SL et al., 2021. SARS-CoV-2 infection and longitudinal fecal screening in Malayan tigers (Panthera tigris jacksoni), Amur tigers (Panthera tigris altaica), and African lions (Panthera leo krugeri) at the Bronx Zoo, New York, USA. Journal of Zoo and Wildlife Medicine 51(4): 733-44.

Barua S et al., 2021. Antibodies to SARS-CoV-2 in dogs and cats, USA. Emerging Microbes and Infections 10(1): 1669-74.

Bengis RG et al., 2004. The role of wildlife in emerging and re-emerging zoonoses. Revue scientifique et technique-office international des epizooties 23(2): 497-512.

Bessière P et al., 2021. Household cases suggest that cats belonging to owners with COVID-19 have a limited role in virus transmission. Viruses 13: 673.

Bosco-Lauth AM et al., 2020. Experimental infection of domestic dogs and cats with SARS-CoV-2: Pathogenesis, transmission, and response to reexposure in cats. Proceedings of the National Academy of Sciences 117(42): 26382-8.

Bosco-Lauth AM et al., 2021. Peridomestic Mammal Susceptibility to Severe Acute Respiratory Syndrome Coronavirus 2 Infection. Emerging Infectious Diseases 27: 2073–2080.

Bosco-Lauth AM et al., 2021. Susceptibility of livestock to SARS-CoV-2 infection. Emerging Microbes and Infections 10(1): 2199-201.

Braun KM et al., 2021. Transmission of SARS-CoV-2 in domestic cats imposes a narrow bottleneck. PLoS Pathogens 17: e1009373.

Brüssow H, 2023. Viral infections at the animal–human interface—Learning lessons from the SARS-CoV-2 pandemic. Microbial Biotechnology.

Chaintoutis SC et al., 2021. Limited cross-species transmission and absence of mutations associated with SARS-CoV-2 adaptation in cats: A case study of infection in a small household setting. Transboundary and Emerging Diseases 69: 1606–1616.

Chan JF et al., 2020. Simulation of the clinical and pathological manifestations of coronavirus disease 2019 (COVID-19) in a golden Syrian hamster model: implications for disease pathogenesis and transmissibility. Clinical Infectious Diseases 71(9): 2428-46.

Chouchane L et al., 2021. Dromedary camels as a natural source of neutralizing nanobodies against SARS-CoV-2. JCI insight 3: 6(5).

Cool K et al., 2022. Infection and transmission of ancestral SARS-CoV-2 and its alpha variant in pregnant white-tailed deer. Emerging Microbes and Infections 11(1): 95-112.

Curukoglu A et al., 2021. First direct human-to-cat transmission of the SARS-CoV-2 B.1.1.7 variant. Australian Veterinary Journal 99: 482–488.

Decaro N et al., 2021. SARS-CoV-2 infection in dogs and cats: facts and speculations. Frontiers in Veterinary Science 8: 619207.

Deng J et al., 2020. SARS-CoV-2 Serological Survey of Cats in China before and after the Pandemic. Virologica Sinica 35(6): 846-8.

Deng W et al., 2020. Primary exposure to SARS-CoV-2 protects against reinfection in rhesus macaques. Science 369(6505): 818-23.

Dhama K et al., 2020. SARS-CoV-2 jumping the species barrier: Zoonotic lessons from SARS, MERS and recent advances to combat this pandemic virus. Travel Medicine and Infectious Disease 37: 101830.

Domańska-Blicharz K et al., 2021. Mink SARS-CoV-2 infection in Poland–short communication. Journal of Veterinary Research 65(1): 1.

Dróżdż M et al., 2021. Current state of knowledge about role of pets in zoonotic transmission of SARS-CoV-2. Viruses 13(6): 1149.

EFSA Panel on Animal Health and Welfare, 2023. SARS-CoV-2 in animals: susceptibility of animal species, risk for animal and public health, monitoring, prevention and control. EFSA Journal 21(2): e07822.

Fenollar F et al., 2021. Mink, SARS-CoV-2, and the human-animal interface. Frontiers in Microbiology 12: 663815.

Fischhoff IR et al., 2021. Predicting the zoonotic capacity of mammals to transmit SARS-CoV-2. Proceedings of the Royal Society B 288(1963): 20211651.

Fritz M et al., 2020. High prevalence of SARS-CoV-2 antibodies in pets from COVID-19+ households. One Health 11: 100192.

Fritz M et al., 2022. First evidence of natural SARS-CoV-2 infection in domestic rabbits. Veterinary Sciences 9(2): 49.

Garigliany M et al., 2020. SARS-CoV-2 natural transmission from human to cat, Belgium, March 2020. Emerging infectious diseases 26(12): 3069.

Gaudreault NN et al., 2022a. SARS-CoV-2 infection, disease and transmission in domestic cats. Emerging Microbes and Infections 9: 2322–2332.

Gaudreault NN et al., 2022b. Susceptibility of sheep to experimental co-infection with the ancestral lineage of SARS-CoV-2 and its alpha variant. Emerging Microbes and Infections 11(1): 662-75.

Giner J et al., 2021. SARS-CoV-2 seroprevalence in household domestic ferrets (Mustela putorius furo). Animals 11(3): 667.

Gonçalves A et al., 2021. SARS-CoV-2 viral dynamics in non-human primates. PLoS Computational Biology 17(3): e1008785.

Goraichuk IV et al., 2021. Zoonotic and reverse zoonotic transmissibility of SARS-CoV-2. Virus Research 302: 198473.

Gortazar C et al., 2021. Natural SARS-CoV-2 Infection in Kept Ferrets, Spain. Emerging Infectious Diseases 27: 1994–1996.

Grome HN et al., 2022. SARS-CoV-2 outbreak among Malayan tigers and humans, Tennessee, USA, 2020. Emerging Infectious Diseases 28(4): 833.

Halfmann PJ et al., 2020. Transmission of SARS-CoV-2 in Domestic Cats. The New England Journal of Medicine 383: 592–594.

Hammer AS et al., 2021. SARS-CoV-2 transmission between mink (Neovison vison) and humans, Denmark. Emerging infectious diseases 27(2): 547.

Hedman HD et al., 2021. Host diversity and potential transmission pathways of SARS-CoV-2 at the human-animal interface. Pathogens 10(2): 180.

Hong J et al., 2022. Dromedary camel nanobodies broadly neutralize SARS-CoV-2 variants. Proceedings of the National Academy of Sciences 119(18): e2201433119.

Hosie MJ et al., 2021. Detection of SARS-CoV-2 in respiratory samples from cats in the UK associated with human-to-cat transmission. Veterinary Record 188: e247.

Hossain MG et al., 2021. SARS-CoV-2 host diversity: An update of natural infections and experimental evidence. Journal of Microbiology, Immunology and Infection 54(2): 175-81.

Hu B et al., 2021. Characteristics of SARS-CoV-2 and COVID-19. Nature Reviews Microbiology 19(3): 141-54.

Huang YJ et al., 2020. SARS-CoV-2 failure to infect or replicate in mosquitoes: an extreme challenge. Scientific Reports 10(1): 11915.

Kane Y et al., 2023. Animal Models, Zoonotic Reservoirs, and Cross-Species Transmission of Emerging Human-Infecting Coronaviruses. Annual Review of Animal Biosciences 11: 1-31.

Klaus J et al., 2021. Detection and Genome Sequencing of SARS-CoV-2 in a Domestic Cat with Respiratory Signs in Switzerland. Viruses 13: 496.

Kumar V et al., 2020. SARS-CoV-2 (COVID-19): zoonotic origin and susceptibility of domestic and wild animals. Journal of Pure and Applied Microbiology 14(1): 741-7.

Leroy EM et al., 2020. The risk of SARS-CoV-2 transmission to pets and other wild and domestic animals strongly mandates a one-health strategy to control the COVID-19 pandemic. One Health 10: 100133.

Letko M et al., 2020. Bat-borne virus diversity, spillover and emergence. Nature Reviews Microbiology 18(8): 461-71.

Lim YX et al., 2016. Human coronaviruses: a review of virus–host interactions. Diseases 4(3): 26.

Liu P et al., 2020. Are pangolins the intermediate host of the 2019 novel coronavirus (SARS-CoV-2)? PLoS Pathogens 16(5): e1008421.

Liu Y et al., 2021. Functional and genetic analysis of viral receptor ACE2 orthologs reveals a broad potential host range of SARS-CoV-2. Proceedings of the National Academy of Sciences 118(12): e2025373118.

Lu L et al., 2021. Adaptation, spread and transmission of SARS-CoV-2 in farmed minks and associated humans in the Netherlands. Nature Communications 12(1): 6802.

Luan J et al., 2020. Spike protein recognition of mammalian ACE2 predicts the host range and an optimized ACE2 for SARS-CoV-2 infection. Biochemical and Biophysical Research Communications 526(1): 165-9.

Magouras I et al., 2020. Emerging zoonotic diseases: Should we rethink the animal–human interface? Frontiers in Veterinary Science 7: 582743.

McAloose D et al., 2020. From people to Panthera: Natural SARS-CoV-2 infection in tigers and lions at the Bronx Zoo. MBio 11(5): 10-128.

Meekins DA et al., 2020. Susceptibility of swine cells and domestic pigs to SARS-CoV-2. Emerging Microbes and Infections 9(1): 2278-88.

Messenger AM et al., 2014. Reverse zoonotic disease transmission (zooanthroponosis): a systematic review of seldom-documented human biological threats to animals. PloS one 9(2): e89055.

Michelitsch A et al., 2020. Occurrence of antibodies against SARS-CoV-2 in the domestic cat population of Germany. Vaccines 8: 772.

Montes A et al., 2020. Can house flies mechanically carry and/or transport sars-cov-2? International Journal of Clinical Virology 4(1): 076-8.

Munster VJ et al., 2020. Respiratory disease in rhesus macaques inoculated with SARS-CoV-2. Nature 585(7824): 268-72.

Mykytyn AZ et al., 2021. Susceptibility of rabbits to SARS-CoV-2. Emerging Microbes and Infections 10(1): 1-7.

Neira V et al., 2021. A household case evidences shorter shedding of SARS-CoV-2 in naturally infected cats compared to their human owners. Emerging Microbes and Infections 10: 376–383.

Nekoei S et al., 2022. SARS-CoV-2 Transmission by arthropod vectors: A scoping review. BioMed Research International 8: 2022.

Olival KJ et al., 2020. Possibility for reverse zoonotic transmission of SARS-CoV-2 to free-ranging wildlife: A case study of bats. PLoS Pathogens 16(9): e1008758.

Oreshkova N et al., 2020. SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. Eurosurveillance 25(23): 2001005.

Oude Munnink BB et al., 2021. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. Science 371(6525): 172-7.

Pagani G et al., 2021. Human-to-Cat SARS-CoV-2 Transmission: Case Report and Full-Genome Sequencing from an Infected Pet and Its Owner in Northern Italy. Pathogens 10: 252.

Patterson EI et al., 2020. Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy. Nature Communications 11(1): 6231.

Plowright RK et al., 2017. Pathways to zoonotic spillover. Nature Reviews Microbiology 15(8): 502-10.

Pomorska-Mól M et al., 2021. A cross-sectional retrospective study of SARS-CoV-2 seroprevalence in domestic cats, dogs and rabbits in Poland. BMC Veterinary Research 17: 1-8.

Purves K et al., 2023. First Eurasian cases of SARS-CoV-2 seropositivity in a free-ranging urban population of wild fallow deer. BioRxiv 2023: 2023-07.

Račnik J et al., 2021. Transmission of SARS-CoV-2 from human to domestic ferret. Emerging Infectious Diseases 27(9): 2450.

Ren W et al., 2021. Mutation Y453F in the spike protein of SARS-CoV-2 enhances interaction with the mink ACE2 receptor for host adaption. PLoS Pathogens 17(11): e1010053.

Reuben R et al., 2020. COVID-19: Probable involvement of insects in the mechanical transmission of novel coronavirus (2019-nCoV). Microbes and Infectious Diseases 1(3): 111-7.

Sailleau C et al., 2020. First detection and genome sequencing of SARS-CoV-2 in an infected cat in France. Transboundary and Emerging Diseases 67(6): 2324-8.

Salajegheh Tazerji S et al., 2020. Transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to animals: an updated review. Journal of Translational Medicine 18(1): 1-10.

Schlottau K et al., 2020. SARS-CoV-2 in fruit bats, ferrets, pigs, and chickens: an experimental transmission study. The Lancet Microbe 1(5): e218-25.

Segalés J et al., 2020. Detection of SARS-CoV-2 in a cat owned by a COVID-19− affected patient in Spain. Proceedings of the National Academy of Sciences 117(40): 24790-3.

Segars J et al., 2020. Prior and novel coronaviruses, Coronavirus Disease 2019 (COVID-19), and human reproduction: what is known? Fertility and Sterility 113(6): 1140-9.

Shi J et al., 2020. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS–coronavirus 2. Science 368(6494): 1016-20.

Sit TH 2020. Infection of dogs with SARS-CoV-2. Nature 586(7831): 776-8.

Suarez DL et al., 2020. Lack of Susceptibility to SARS-CoV-2 and MERS-CoV in Poultry. Emerging Infectious Diseases 26: 3074–3076.

Sun SH et al., 2020. A mouse model of SARS-CoV-2 infection and pathogenesis. Cell Host and Microbe 28(1): 124-33.

Udom K et al., 2022. Serological survey of antibodies against SARS-CoV-2 in dogs and cats, Thailand. Transboundary and Emerging Diseases 69(4): 2140-7.

Ul-Rahman A, 2020. A comparative phylogenomic analysis of SARS-CoV-2 strains reported from non-human mammalian species and environmental samples. Molecular Biology Reports 47(11): 9207-17.

Ulrich L, 2020. Experimental infection of cattle with SARS-CoV-2. Emerging Infectious Diseases 26(12): 2979.

Van Aart AE et al., 2022. SARS-CoV-2 infection in cats and dogs in infected mink farms. Transboundary and Emerging Diseases 69(5): 3001-7.

Xia H et al., 2020. SARS-CoV-2 does not replicate in Aedes mosquito cells nor present in field-caught mosquitoes from Wuhan. Virologica Sinica 35: 355-8.

Xu J et al., 2021. Nanobodies from camelid mice and llamas neutralize SARS-CoV-2 variants. Nature 595(7866): 278-82.

Yen HL et al., 2022. Transmission of SARS-CoV-2 delta variant (AY. 127) from pet hamsters to humans, leading to onward human-to-human transmission: a case study. The Lancet 399(10329): 1070-8.

Zhang Q et al., 2020. SARS-CoV-2 neutralizing serum antibodies in cats: a serological investigation. BioRxiv 3: 2020-04.

Zhao J et al., 2020. The potential intermediate hosts for SARS-CoV-2. Frontiers in Microbiology 11: 580137.

Zhou P and Shi ZL, 2021. SARS-CoV-2 spillover events. Science 371(6525): 120-2.

Zoccola R et al., 2021. First detection of an Italian human-to-cat outbreak of SARS-CoV-2 Alpha variant—lineage B.1.1.7. One Health 13: 100295.