

Current State of SARS-CoV-2 Infection in Capreolus and Cervid Species and the Potential of Future Zoonosis

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ABSTRACT

The rapidly spreading Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has inflicted numerous patients and deaths in human inhabiting city-states worldwide. Due to its zoonotic nature, not only humans are susceptible to the recent threat. Non-human wildlife such as white-tailed deer (*Odocoileus virginianus*), the Père David's deer (*Elaphurus davidianus*), and the typical roe deer (*Capreolus capreolus*) are all highly susceptible to SARS-CoV-2 due to the virus targeting highly conserved genes such as host angiotensin-converting enzyme 2 (ACE-2) receptors. While the virus was vastly spreading globally within human patients, wildlife was also contacted via viral residue discarded in local cities or direct contact with infected patients. The current situation of cervids and capreolus species are reported to be inflicted by SARS-CoV-2 vastly throughout multiple countries. The ability to contain the coronavirus and act as both a reservoir and a method to successfully transmission the virus vertically to future generations will indefinitely enable SARS-CoV-2 to develop novel mutations and in turn unleash another possible zoonotic outbreak.

Keywords: SARS-CoV-2; Wildlife; Human; Cervid; Zoonosis

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a positive sense single-stranded RNA virus that constantly threatens the public health [1]. After the initial identification, the pandemic had spread to regions far across its originated continent claiming more than 5.9 million deaths and infecting more than 433 million people around the world [2]. The infection alone did not lead the virus as a global threat. The ability to transform into multiple subtype variants due to its RNA nature made governments and health care departments more challenging to successfully identify and cure infected patients. While the current state of SARS-CoV-2 is a major concern, the event of its emergence is also important because the transmission itself was zoonotic. SARS-CoV-2 is categorized within the severe acute respiratory syndrome related Coronavirus (SARSr-CoV) of the family Coronaviridae [3]. In attempts to discover which animal started the infection, reports indicated a genome sequence of one of the SARSr-CoV which

resembled 96% of the whole RaTG13 gene within SARS-CoV-2 [4]. The report suggested hard evidence of viral genome sequences from bats were the origin of the initial infection. Since the report was released, several other bat viral genome sequences related to SARS-CoV-2 have been sighted from different regions in China and Japan [5-8]. Considering previous reports, it may have been inevitable of cross-infection of the SARS-CoV-2 virus from non-human mammals. As the infection continue among the human population, other mammals were also in the risk of exposure by any contacts with human patients. SARS-CoV-2 targets the host angiotensin-converting enzyme 2 (ACE-2) receptor to tether cells [9]. Interestingly, ACE-2 receptor are highly conserved genes which are observed in various animal species [10]. As a result, various incidents regarding dogs, cats, zoo animals, and even farmed minks were documented as a SARS-CoV-2 infection [11-14]. While domestic and industrial mammals were the first to be infected

due to numerous human contacts, the continuous widespread has led to further spillovers regarding local wildlife [15]. Among the indigenous wildlife, capreolus and cervid species were reported to be highly susceptible to SARS-CoV-2, especially white-tailed deer (*Odocoileus virginianus*), the Père David's deer (*Elaphurus davidianus*), and the typical roe deer (*Capreolus capreolus*) [16]. This review is to aim on the current SARS-CoV-2 situation in wild capreolus and cervid species and the potential zoonotic backlash it will bring to human public health care.

Methods of Transmission from Human to Wildlife

When compared to local domestic and industrial animals, wildlife located far from suburbs are considered less hazardous to confront direct SARS-CoV-2 infection. However, reports suggest a high possibility that infected patients shed SARS-CoV-2 within feces [17]. Recent research on other Coronavirus subtypes such as Middle East Respiratory Syndrome (MERS) report detection rates of 14.6% and 2.4% within fecal and urine samples [18]. The predecessor SARS-CoV inflicted patients experienced diarrhea and SARS-CoV RNA was detected within the stool samples and small intestines [19]. The SARS-CoV virus was able to remain contact and fully functional in diarrheal samples for a maximum 4 days at room temperature [20]. Similar to its former subtypes, a recent report discovered a U. S. patient infected with SARS-CoV-2 shed SARS-CoV-2 RNA in their feces [21]. More than 50% 96 patients'

feces samples collected over 31 days detected SARS-CoV-2 [22]. The research proves that a portion of the infected patients are able to shed SARS-CoV-2 virus via diarrheal feces. The disposed virus derived from populated suburbs, hospitals, and airports will be transported to various sewage systems. Mistreated water has the potential to carry SARS-CoV-2 RNA and act as a potential vehicle to expose the virus directly to the natural aquatic environment [23-25]. Coronavirus has been known to lose its initial infectivity when exposed in water due to its lipid envelope structure [26]. However, depending on the viral subtype and condition of the water such as temperature, Human derived Coronavirus are known to survive more than 500 days [27]. This provides ample time for wandering roe deer and other cervids to be contacted by the virus and be infected via the gastrointestinal organs. The other major method of a spillover would be due to seasonal hunting. Studies regarding retropharyngeal lymph node samples of wild deer discovered a sharp increase in positive SARS-CoV-2 RNA signatures when the hunting season started on September 19, 2020, until January 10, 2021 [28]. The study in Iowa suggests major influx of people during the hunting season left various SARS-CoV-2 containing residue infecting the Southeastern area (Figure 1) Suresh V. Kuchipudi, et al. [28]. The virus contacted deer acted as a viral reservoir to actively spread to other regions, gradually infecting in all directions. This state limited situation later developed to regional crossing inflicting SARS-CoV-2 infection in other states.

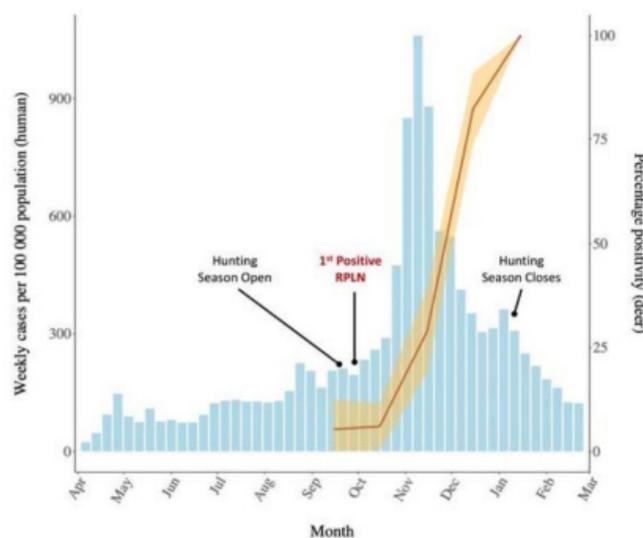


Figure 1: Epidemic curve showing SARS-CoV-2 weekly cases (per 100,000) in humans and the monthly change in SARS-CoV-2 positivity in White-tailed deer in Iowa. Adapted from Multiple spillovers and onward transmission of SARS-Cov-2 in free-living and captive White-tailed deer (*Odocoileus virginianus*) by Suresh V. Kuchipudi, 2022, Proc Natl Acad Sci 119(6).

Current State of Capreolus and Cervid Species Infection

While SARS-CoV-2 was widespread in major human populated regions, SARS-CoV-2 wildlife dissemination were not yet sighted. The trend of the viral infection tends to have a gap of one year in the viral progression. As of today, situation of SARS-CoV-2 infecting various cervid and capreolus species is spotted in almost every continent. Vast samples of deer originating from different countries in North America such as Ohio and Maryland in the United States and Canada have detected SARS-CoV-2 RNA [29]. SARS-CoV-2 detection efforts are also increased in Eurasian countries such as northern Fennoscandia, Iceland, and Eastern Russia [30]. Compared to the western regions, reports regarding cervid and capreolus species inhabiting eastern countries are relatively short. Main reports are focused on the direct culprit which started the viral outbreak. Japan, China, and Singapore reported positive identification of the same SARS-CoV-2 strand containing bats. This strongly predicts there will be high chance of local deer or other capreolus species exposed to SARS-CoV-2 residue and naturally be infected.

Viral Characteristics and Variants among the Infected Cervid Species

SARS-CoV-2 drastically developed within the human patients by transforming through a series of mutations later discovered as novel variants of the original virus. Within 2019 to 2022, major SNP mutations named as Alpha, Beta, Gamma, Delta, and

the latest Omicron variant quickly spread to heavily populated human settlements. Similarly, local wildlife has also contacted the gradually mutating virus. It is crucial for both the infected deer and human patient to be identified which subtype of SARS-CoV-2 as every variant mostly contains variant specific point mutations. For example, the previous alpha variant was identified as a novel variant due to mutations such as N501Y, D614G, and P681H. This enabled the mutated spike proteins of SARS-CoV-2 to improve its ability to bind cellular receptors of host cells [31]. The more recent variant Delta and Omicron contained more unique point mutations such as the T478K, P681R, and K417N mutation in Delta and E484D, P812R, and Q954H in Omicron variants [32,33]. While the alpha and other previously found variants are hindering within the human population, wild deer and other capreolus species are in the relatively early stages of dissemination. What is more concerning with the infected deer is that not only does the animals act as a suitable reservoir for SARS-CoV-2, but also the ability to transmission the virus from doe to fetus. Recent reports suggest adult white-tailed deer can transmit the Alpha variant of SARS-CoV-2 vertically [34]. The virus's ability of vertical transmission in utero have been documented in human pregnant patients [35], but the ability of other wildlife mammals to pass on previous variants will indefinitely influence future SARS-CoV-2 development. Infected cervids will contain the virus through generations and may eventually harbor novel mutations that will in turn trigger yet another zoonosis to unsuspecting humans (Figure 2).

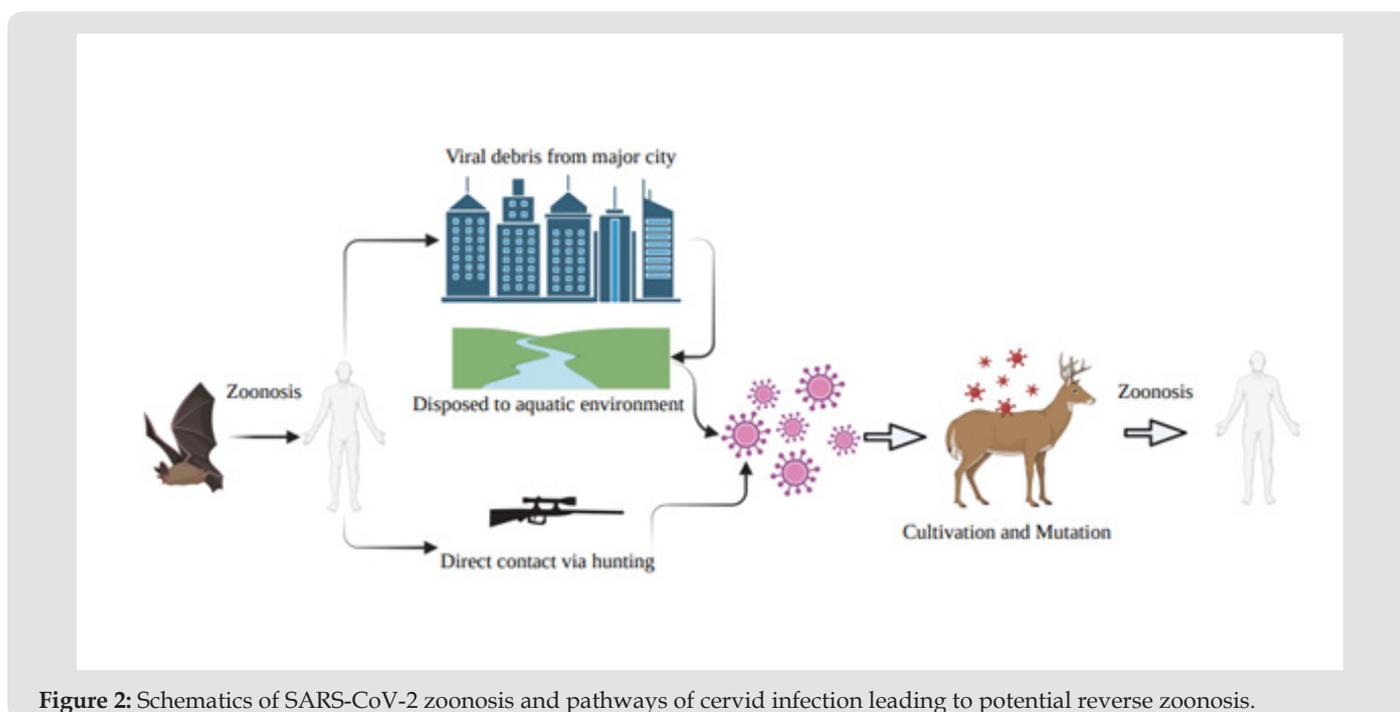


Figure 2: Schematics of SARS-CoV-2 zoonosis and pathways of cervid infection leading to potential reverse zoonosis.

Conclusion

Studies regarding the current spread of SARS-CoV-2 infection in wild cervid or capreolus species are yet to be finished. Further sequencing and observation will be required to successfully document how far wildlife have been exposed to the zoonotic virus that may prevent another, perhaps more serious outbreak of reverse zoonosis.

Declarations

Ethical Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Data Availability Statement

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Competing Interests

The author declares no competing interests.

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Authors' Contributions

Hyoung-Min Park contributed in review design, manuscript writing, and overall process.

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