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COVID-19: Zoonotic potentials, viral structure encouraging its mechanism for inter-host transmission and its potential risk for Veterinarians, Animal handlers, Zoo-Keepers and Pet-Owners: Review

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Abstract: COVID-19, caused by SAR- CoV-2 virus and a worldwide disease pandemic was first reported in Wuhan, China as a disease outbreak and afterwards it has rapidly spread from China to more than 216 countries, with 100,893,336 reported cases since the first report and 2, 168, 723 mortalities worldwide as of January 27, 2020. SARS-CoV-2, the aetiologic virus is thought to emanate from bats; however, information about the intermediate animal sources of the virus still remains unclear. There have been reports of COVID-19 infection in animals and this gives credence to the zoonotic potentials of this deadly virus. In this mini-review, we evaluate the zoonotic potentials of COVID-19, the viral structure and mechanism that will likely favor COVID-19 inter-hosts transmission, it's potential risk for Veterinarians, Animal handlers, Zoo-Keepers and Pet-Owners. In Conclusion, there are no concrete scientific evidence that the animals infected with COVID-19 infection can transmit same virus to human beings but recommend that Veterinarians, Animal care givers and Zoo keepers to every caution and safety measures possible when in close proximity with these animals, sufficient restriction of movement and provision of animals needs for these pets, who can wander and get infected by contact with Humans with COVID-19 infection and we encourage a One-health approach and synergy between health professionals including Vets to tackle and contain this scourge.

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Introduction

Emerging zoonotic viruses have evinced to be some of the fatal and pernicious diseases known (Ahmad *et al.,* 2020a; Rodriguez-Morales *et al.,* 2020a). COVID-19, is a major part of this set of diseases (Ahmad *et al.,* 2020*a*) and is thought to be contracted from the animals, although it is not yet distinctly described from which animal it was transmitted from (Ahmad *et al.,* 2020a).

Coronaviruses are the aetiology of a number of maladies in humans and animals (Biscayart et al., 2020). The first report of COVID-19 (a coronavirus) outbreak was in the city of Wuhan, Hubei province (Ahmad *et al.,* 2020a & b; Biscayart et al., 2020; Mahdy, 2020; Rodriguez-Morales *et al.,* 2020). On December 12, 2019, the Wuhan Municipal Health Commission (WMHC) reported that 27 persons were infected by a new coronavirus which was initially known as 2019-novel coronavirus (2019-nCoV), and later as Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO) (Salata *et al.*, 2019; Ahmad *et al*., 2020a). This disease is caused by SARS-COV-2 (da Costa *et al*., 2020; Guo *et al.,* 2020). Seven (7) of the recorded cases were gravely sick and had a medical history of exposure with the Seafood Wholesale Market (Ahmad *et al*., 2020a; Mahdy, 2020). This Seafood market located at Wuhan, had different types of wild (snakes, bats and marmots) and farm (poultry) animals unlawfully sold (Ahmad et al*., 2020*a; Lorusso *et al.,* 2020). The outbreak that followed the initially reported cases was linked epidemiologically to this market (Mackenzie and Smith, 2020). Therefore, this disease might be an emerging infectious zoonotic disease because it might

be passed on from animals to humans (Ahmad et al., 2020; Tiwari *et al*, 2020).

From the time of the first report of the outbreak of this deadly virus in Wuhan, China, it has rapidly spread from China to more than 216 countries, involving more than 31,000 confirmed cases with 638 deaths in the first month to 100,893,336 confirmed cases since the first report and 2, 168, 723 deaths globally as of January 27, 2021 (Salata *et al.,* 2019; Torti *et al*., 2020; ECDC, WHO, 2020a; Worldometer, 2021).

COVID-19, has continued to spread, despite the tremendous efforts to constrain this virus and control the disease, leading to an epidemic of global dimensions (Tiwari *et al.,* 2020). SARS-CoV-2 is speculated to have come from bats; however, the intermediate animal sources of the virus remains unidentified and unrecognized (Shi *et al.,* 2020). There have been reports of COVID-19 infection in animals (AVMA, 2020). Shi *et al*. 2020, reported that SARS-CoV-2 replicates poorly in dogs, pigs, chickens, and ducks, but successfully in ferrets and cats. SARS-CoV-2 mode of transmission in cats is through respiratory droplets (Shi *et al.,* 2020).

The current COVID-19 outbreak has again validated the capabilities of the animal-human disease transmission link and acts as the cardinal origin of emerging zoonotic diseases (Tiwari *et al.,* 2020). Although, deduced data suggests the potential prospect of an initial zoonotic emergence, it is overearly to make concluding statements about the role of intermediate hosts such as wild animals in the origin of SARS-CoV-2, in addition to bats and dromedary camels the natural hosts of other coronaviruses such as SARS-CoV in 2002 and MERS-CoV in 2012 (Ugochukwu *et al.,* 2019; Guo *et al*., 2020; Tiwari *et al.,* 2020).

Zoonotic potential of COVID-19 and mechanism of inter-hosts transmission.

Coronaviruses (CoVs) are critically serious viruses, mostly linked to respiratory and alimentary tract infections of humans and animals (Chen *et al*., 2020; Pal *et al*., 2020). Coronaviruses are helically symmetrical enveloped viruses with a diameter of 100–160 nm (Fehr and Perlman, 2015; Chen *et al*., 2020). Each particle contains a single-stranded RNA genome of 27–32 kb that combines with the nucleoprotein. Viral envelope includes three different proteins: membrane, envelope and spike proteins (Chen *et al*., 2020; Salata *et al*., 2020).

It is important to note that, coronaviruses have crossed the species barrier twice in the past twenty years, and thus SARS-CoV-2 looks to be as a result of species barrier jumping for the third time (Rothan and Byrareddy 2020). Amongst Coronaviruses, recent zoonotic ones such as SARS-CoV, MERS-CoV, and SARS-CoV-2 gained greater relevance due to the severity of disease in humans and because they give rise to a global public health threat (da Costa *et al*., 2020; Rothan and Byrareddy 2020).

The evolution of novel Coronaviruses, their extensive host range and mechanism of their transmission may be due to fluctuations in the levels of replicase, RNA dependent RNA polymerase, polybasic furin cleavage site, and O-linked glycans, proofreading mechanism deficiency, high levels of mutations in the receptor-binding domain of spike gene and genetic recombination (Su *et al*., 2016; Graepel *et al.,*2017; Cui *et al*., 2019; Chen 2020; Patel and Jernigan 2020; Tiwari *et al*., 2020). Research shows that SARS-CoV and SARS-CoV-2 (2019-nCoV) both use the Angiotensin-converting enzyme 2 (ACE2) as a related cell entry receptor for the two viruses (Zhou et al. 2020a; Tiwari *et al.,* 2020).

The phylogenetic sequence of 2019-nCoV RBD gives credence to this, including its receptor-binding motif (RBM) that has direct contact to ACE2, is similar to that of SARS-CoV, and mostly are disseminated through the respiratory tract and strongly prompting the view that 2019-nCoV uses ACE2 as its receptor (Guo *et al*., 2020; Wan *et al*., 2020). Because of the mutation in the RBD region of S gene of Coronaviruses, there is increase in the number of hosts susceptible to these viruses, leading to increase in its pathogenicity thus, becoming a matter of worldwide concern and apprehension (Chen 2020; Patel and Jernigan 2020; Tiwari *et al*., 2020; Wan *et al*., 2020).

In recent times, some animals (Bats, Civets and Camels) have been incriminated as the animal carriers of human Coronavirus infections (Cui et al. 2019). Of the latest, bats (Wu et al. 2020b) and pangolins (Zhang et al. 2020a) are considered to be the probable sources of origin of SARS-CoV-2 (Andersen et al. 2020). However, phylogenetic analysis has only indicated a bat origin of 2019-nCoV, 2019-nCoV and also potentially recognizes ACE2 from a wide range of heterogeneous animal species (except mice and rats), implicating these animal species as possible intermediate hosts or animal models for 2019-nCoV infections (Wan *et al.,* 2020). Here is the basis for suspicion of the presence of an intermediate non-human host that is culpable for the zoonotic spilling over to the human populations (Weiss and Leibowitz, 2011; Murdoch and French 2020; Oreshkova *et al*., 2020).

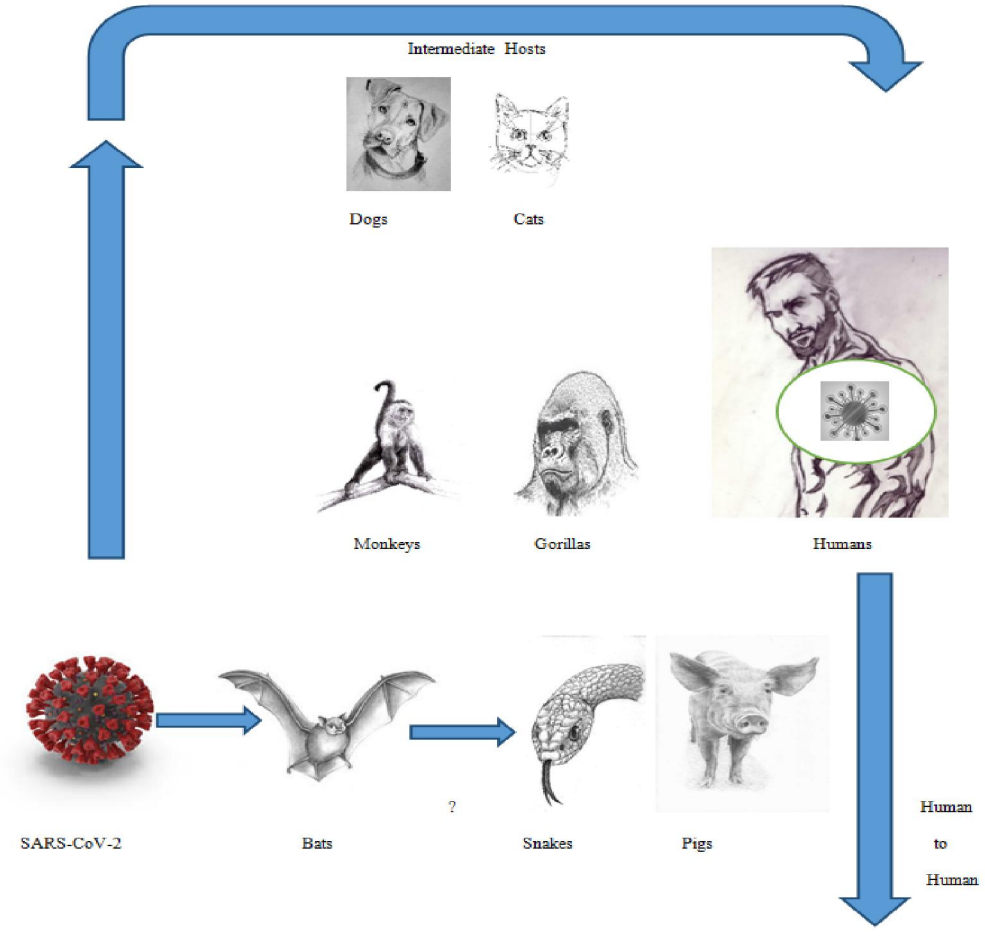
COVID-19 and it's potential risk for Veterinarians, Animal handlers, Zoo-Keepers and Pet-Owners

COVID-19 the recent worldwide pandemic was first identified in sick patients in Wuhan, who had association with the Huanan seafood wholesale market and this suggests a possible zoonotic link (Mahdy, 2020; Tiwari *et al.,*2020; Zhai *et al*., 2020). So,

animals have been identified as the sources of COVID-19 dissemination as described in Figure 1 (Ahmad *et al.,* 2020a). However, till now, very few animals have been reported positive for SARS-CoV-2 infection globally (AVMA, 2020) as shown in Table 1.

COVID-19 infection has been recorded in two dogs from Hong Kong (Almendros 2020a). The first case was reported in a 17-year-old Pomeranian dog whose oronasal samples subjected to RT-PCR analysis were positive for COVID-19 (Almendros 2020a; Almendros and Gascoigne 2020a; AVMA, 2020; Tiwari *et al*., 2020). Then as well, another case of COVID-19 infection in a German Shepherd Dog in Hong Kong was recorded. It is striking to report that both cases of canine COVID-19 infections were reported in dogs living in close proximity with COVID-19 positive owners (AVMA, 2020; Tiwari et al*.,* 2020). But till now, there is no concrete scientific proof that dogs get COVID-19 infection from, or can transmit this virus to humans (Almendros, 2020a).

There are reports of feline COVID-19 infection from Belgium and Hong Kong (AVMA, 2020). Reports from Harbin Veterinary Research Institute show that cats get infected under experimental situations and can spread to other susceptible cats housed together (Mallapaty 2020; Shi *et al*., 2020). The findings are based on experimental infection and under natural conditions may not produce same results (Tiwari *et al*., 2020). However, a serological study conducted among the cats from the Wuhan Province in China showed the presence of SARS-CoV-2 neutralizing antibodies (Tiwari *et al*., 2020; Zhang *et al*., 2020b). This findings thus indicates that cats can get SARS-CoV-2 infection under natural conditions and this elicits an antigen-antibody reaction (Zhang et al. 2020b). However, among the cats that tested positive, higher antibody titre levels were recorded in the cats living in close proximity with COVID-19 infected pet owners (Zhang et al. 2020b). However, the possible role of cats in the epidemiology of COVID-19 is something that needs further investigation; so feline COVID-19 infection could present a case of anthropozoonosis. This, obviously, does not rule out the need to prevent human exposure to these infected domesticated cats or other pets. Waste matter from infected stray cats may in theory, have a hand in environmental contamination (McNamara *et al.,* 2020).



Fish Camel
Intermediate Host
Figure 1-Potential transmission routes of SARS-CoV2 (Ahmad *et al.,* 2020a)

In Zoo animals, a Malayan tiger kept in the Bronx Zoo of New York City, USA recently tested positive for SARS-CoV-2 after they started showing mild respiratory signs. There was suspicion of this animal been infected by a COVID-19 infected zookeeper not showing clinical signs (Tiwari *et al*., 2020; USDA, 2020).

Between January 1– June 8, 2020, the first five months of COVID-19 outbreak, not fewer than 20 pets all over the globe have been diagnosed with this deadly virus. This, in spite of the growing numbers of COVID-19 confirmed case in humans globally (AVMA, 2020). Notwithstanding, none of these reports suggest that pets are a source of infection for humans. Documented reports till date from the few domestic animals that have tested positive for SARS-CoV-2 indicate these infection were due to close contact with people with COVID-19 (AVMA, 2020; Tiwari *et al*., 2020).

On April 26, Holland's Minister of Agriculture, Nature, and Food Quality, reported in a communication to the Dutch parliament that several minks on each of two large farms had tested positive for the aetiologic viral agent of COVID-19. Animal care givers at each of these farms had developed clinical symptoms of COVID-19. It is believed that these caretakers transmitted the virus to the minks (AVMA; 2020; CDC, 2020).

Table 1- Chronological sequence and geographical location of the diagnoses of animals with COVID-19

Date reported	Animal species	Country of diagnosis	References
March 6. 2020	Dog	Hong Kong	Simin *et al*., 2020
(Pomeranian dog)			
March 19, 2020	Dog	Hong Kong	McNamara *et al*.,2020
(German Shephard)			
March 27, 2020	Cat	Belgium	Brown 2020, Bryner 2020; AVMA, 2020
April 3	Stray and Housed	(Wuhan) China	Zhang, 2020b
Cats (about 15)			
April 18	Cats (2)	USA (New York)	Zhang, 2020b
April, 19	Malayan tiger	USA (Bronx Zoo)	McNamara *et al*., 2020
April, 26	Minks	Netherlands	AVMA, 2020
January,11, 2021	Gorillas (3)	USA (San Diego, CA)	USDA, 2021
January,19, 2021	Ferret	Slovenia	CDC, 2021
January,19, 2021	Puma	South Africa	CDC, 2021

However, On May 25, the Minister reported that based on initial sequence analyses and phylogenetic mapping, it was possible that in at least two cases, the virus was transmitted from an infected mink to a susceptible human host (AVMA, 2020; Oreshkova *et al*., 2020). More research is being done to better discern whether interspecies transmission of SARS-CoV-2 between mink and humans could take place. Additionally, seven of 24 farm cats were found to have circulating antibodies specific for SARS-CoV-2, indicating previous infection with the virus (AVMA, 2020). COVID-19 was also reported in a ferret and Puma in Slovenia and South Africa respectively (CDC, 2021).

On 11th of January, 2021, National Veterinary Services Laboratories (NVSL) of the United States Department of Agriculture's (USDA) diagnosed SARS-CoV-2 in three gorillas at the San Diego Zoo, California (USDA, 2021)

These recent reportage of SARS-CoV-2 in animals have led to superfluous panic among the general public as well as pet owners and have negatively influenced the welfare of animals (Parry, 2020; Tiwari *et al*., 2020). But presently, there is no concrete information or clues that domesticated animals play a significant role in spreading the virus SARS-COV-2 to humans including veterinarians, animal handlers, Zoo-Keepers and Pet-Owners (CDC, 2020).

Recommendations

The first confirmed reports of pets infected with SARS-CoV-2 came from Hong Kong. From the outset of this outbreak there, the government in conjunction with the Agriculture, Fisheries, and Conservation Department (AFCD) recommended that mammalian pets from households with persons with COVID-19 infection be quarantined, tested and taken care of (AVMA, 2020). It is also recommended for pet-owners, to prevent pets from interacting with people or other animals outside the household; keeping pets indoors, and possibly withholding them from interacting with other animals or people; walking dogs on a leash, keeping at least a 6 feet social distance from other people and animals; and avoiding dog parks or public places where a large number of people and dogs gather (AVMA, 2020).

Continual human-animal contacts either in the market or where animal are kept without using proper biosecurity were pointed out as significant zoonosis spread risk factors (Daszak *et al.,* 2020). It is very paramount to understand the susceptibility of animals to SARS-CoV-2 in order to control COVID-19 (Mahdy, 2020). Therefore, It is also recommended for Veterinarians, Animal care givers and Zoo keepers to avoid any contact with farm or wild animals without the use of personal protective equipment in these days of COVID-19 pandemic (Benvenuto *et al*. 2020). In a one-health approach, there should be greater commitment to drafting surveillance programs and preventive guidelines to have in-depth analysis of bat origin in the past SARS, MERS, and now SARS-CoV-2 epidemic which have grown into pandemic proportions (Daszak *et al*., 2020).

Because of this, intense efforts should be made to contain and control the spread of this emerging virus giving humans a nostalgic feeling and posing a disease of pandemic proportions. Efforts to implement rapid but effective diagnosis, strict and stern vigilance, appropriate isolation, and quarantine procedures for both infected, domestic pets, pet-owners and animal care givers to halt its further spread, increased surveillance, monitoring and contact tracing, proper equipping of medical facilities and intensive care units, networking programs, swift communication and provision of updates, accelerated dissemination of awareness of the related public health risks of this virus to the general populace, intensified efforts to develop effective vaccines. Global collaborative attempts and willingness to fight this pandemic following appropriate One health approach to withstand this emerging virus causing havoc to the lives of billions of the world's population and recently, the animal population are judiciously followed to jointly prevent further transmission and spread (Bonilla-Aldana et al. 2020; Dhama *et al*., 2020; Malik *et al*., 2020; Rodriguez-Morales *et al*., 2020b; Tiwari *et al*.,2020).

In conclusion, scientists and researchers considering pets to be "dead end hosts" (Stone 2020), the risk of animal to human transmission is minimal and that domestic animals are not vectors of this virus, so there is no logic in abandoning animals for fear of contacting the disease while also advising pet owners to exercise extreme caution in handling these animals and pets (Brown, 2020). And, based on the limited empirical information available to date with regards to domestic animals spreading the Virus (SARS-COV-2), the risk of domesticated and zoo animals spreading COVID-19 to people is thought to be very minimal but more research studies are necessary to find out if and how different animals could be affected by COVID-19 and the possibility of their spreading it to Humans (CDC, 2020). In the time being, we recommend, sufficient restriction of movement and provision of animals needs for these pets, who can wander and get infected by contact with Humans with COVID-19 infection. We also encourage a One-health synergistic approach amongst Human medics, Vet medics, Pharmacists, Epidemiologists, Public Health specialists, virologists, Governments across the world and infact all of us to control, contain and defeat the scourge of this pandemic.

Authors' contributions

ICI Ugochukwu and MU Anyanwu conceived the idea, ICI Ugochukwu, MU Anyanwu, NA Sani and R.I. Onoja, prepared the manuscript, while GE Batiha made intellectual contributions. All Authors read and approved the manuscript for submission.

Conflict of interests

The Authors thereby declare that they have no financial or personal interests that may have inappropriately influenced this work.

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