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## Need for veterinarian's intervention in the emerging menace of COVID-19 anthroponosis: A mini review

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### Abstract

Coronavirus disease is the current cause of global concern. The massive outbreak of COVID-19 has led World Health Organization (WHO) to declare this as a pandemic situation. It became the first pandemic by any of the coronaviruses affecting humans or animals. The Severe Acute Respiratory Syndrome Coronavirus-2 (SARSCoV-2) is responsible for COVID-19 leading to acute respiratory distress and substantial mortality. Animals have been an integral part of human life from time immemorial. From providing food, as companion animals to maintaining ecological balance they have had a varied role to play in human life. The laboratory confirmation of the pet dog, being weakly positive to SARS-CoV-2, in Hong Kong has shown human-to-animal transmission (zooanthroponotic) route. Such similar reports of human to other animal species transmission have also been reported in several countries. In this situation the role of veterinarian assumes an important perspective in treating the animals as well as helping in food security, disease diagnosis, surveillance, boosting economy of livestock stakeholders at the grassroot level etc. In the absence of any selective vaccine against SARS-CoV-2, re-purposed drugs are advocated. It is anticipated that the world will triumph over the COVID-19 infection with collaborative, multisectoral, and transdisciplinary approach linking human, animal, and environmental health. The adoption of suitable public health preventive measures and strengthening medical facilities are the best options for managing disease. This review gives an insight into the confirmed SARS-CoV-2 outbreaks in animals, including the factors behind the shuffling of virus among variety of species and the role of veterinarians in managing and safeguarding public health so as to pave the way for adopting one health approach with an aim to conserve biodiversity.

**Keywords:** Veterinarian's, emerging, COVID-19, population

### Introduction

The current global population is going through the worst of its health emergency as every human is either directly or indirectly fighting against the emerging pandemic Corona Virus Disease-2019 (COVID-19). The pandemic caused by a new coronavirus (CoV) was named earlier as 2019 novel Coronavirus (2019-nCoV) (Peeri *et al.*, 2020) [13] but later, on 11th February 2020, its new nomenclature was formulated by the *Coronaviridae* Study Group (CSG) of International Committee on Taxonomy of Viruses (ICTV) as "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)" and the disease was termed as "COVID-19" (Shereen *et al.*, 2020) [16]. Till date (18th May 2020) the total COVID-19 cases in humans counts to 46,19,477 with a case fatality rate of 6.75% (WHO, 2020) [25]. Now the SARS-CoV-2 infection is not only limited to humans, rather its spread crossed the species boundary by affecting different animal species. Although speculations about the origin of this disease has been traced to two different animals: bat and pangolin (Zhou *et al.*, 2020, Zhang *et al.* 2020) [28, 27] marking the disease as zoonotic, ongoing studies are still conducted around the globe to obtain the firm evidence behind the source of virus contraction by human.

CoVs belong to the family *Coronaviridae*, the subfamily *Coronavirinae* and the order *Nidovirales* per the ICTV. On the basis of phylogenetic relationships and genomic structures, four genera - *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus* are grouped under the subfamily *Coronavirinae* (Gorbalenya *et al.*, 2020) [9]. Amid these four genera, mammals can be infected by alpha- and betaCoVs, however gamma- and deltaCoVs infect birds specifically (Wu *et al.*, 2020) [24].

COVID-19 is hypothesized to be stemmed from the clients of the Wuhan's "wet market" (where either live or dead wild animals, reptiles and birds are sold and slaughtered) in Hubei province, China. The first hospitalized case with a mysterious etiology was reported on 8th

Dec 2019. On Jan 7, 2020, a novel CoV was found to be its etiological agent, thereafter WHO declares this as the “public health concern of international emergency” on January 30, 2020 to a pandemic on March 11, 2020 (Wu *et al.*, 2020) [24]. Later the disease spread across the globe affecting the population of 216 countries and territories combinedly as updated on 18th May 2020 (WHO, 2020) [25]. Looking at the spontaneous surge in cases, the question arises whether veterinarians are to be included in the public health management. Nevertheless, many confirmed cases of SARS-CoV-2 in animals are also reported worldwide.

Therefore, this review briefly outlines the veterinary importance of CoVs and summarizes the confirmed cases of SARS-CoV-2 positive animals till date. An attempt has been made to include the factors behind the shuffling of virus among variety of species and the vital role of veterinarians in managing and safeguarding public health.

### Zoonotic perspective

Damas *et al.*, (2020) [5] suggested that bats are the class of mammals which possess the highest acceleration in evolving the acetylcholine esterase-2 (ACE2) receptor for binding to the spike protein of CoV. Hence this mammal represents the primary reservoir for most of the outbreaks in the last two decades. (Hu *et al.*, 2015) [10] has reviewed that bats remained as the natural reservoirs for both SARS-CoV and MERS-CoV, the two high profile human CoV outbreaks in the past, while wild civets and camels were thought to be the intermediate hosts respectively for the transmission of these two viruses to humans. Although the world is still uncertain about the origin of human infection of SARS-CoV-2, significant genetic similarities were claimed to be existing among the CoVs of humans with that of bat and pangolin. Phylogenetic analysis performed by Zhou *et al.*, (2020) [27] found 96.2% identity among the SARS-CoV-2 and RaTG13-CoV of *Rhinolophus affinis* bat from Yunnan province, China at the whole genome level. Later Zhang *et al.* (2020) [26] found 91.02% nucleotide identity among SARS-CoV-2 and the CoV of Malayan pangolins (*Manis javanica*), hence suggesting the animal as an intermediate host for human infection.

Presently the infection is getting transmitted among the humans via droplet infection (Rothan and Byrareddy, 2020) [15]. Many researchers also argue for the existence of faecal-oral transmission of the virus as SARS-CoV-2 have been found in faecal samples of patients (Pan *et al.*, 2020; Wu *et al.*, 2020) [12, 24]. But the spread of disease by animal food consumption is not evident yet.

### Coronavirus disease- veterinary perspective

CoV is a long-established infectious pathogen of veterinary importance. Bovine corona virus affects neonatal, young as well as the adult bovine causing respiratory and the enteric disease (Saif, 2010; Workman *et al.*, 2017) [16, 23]. Feline infectious peritonitis viruses (FIPV) and feline enteric coronaviruses (FECV) are the two biotypes of the Feline coronavirus (FCoV). FECV causes asymptomatic enteric infection in feline, while FIPV causes fatal disease in the domestic as well as in wild Felidae (Vogel *et al.*, 2010) [24]. Canine CoV causes mild self-limiting gastroenteritis in adult dogs while highly virulent strain Pantropic canine corona virus causes lethal systemic infection in the pups (Decaro and Buonavoglia, 2008; Buonavoglia *et al.*, 2006) [6, 2]. Some Corona virus infects dogs can involve tracheobronchitis (Ellis, 2019) [7]. In swine population porcine epidemic diarrhoea

virus (PEDV) and Transmissible gastroenteritis virus (TGEV) belongs to genus *Alphacoronavirus*, which causes severe diarrhoea (Song and Park, 2012) [18]. Corona virus belongs to the genus *Deltacoronavirus* also causes clinical diarrhoea in pigs (Wang *et al.* 2014) [21].

Re-emerging and emerging CoVs include porcine *Deltacoronavirus* (PDCoV) and Porcine epidemic diarrhoea virus (PEDV) and swine acute diarrhoea syndrome-coronavirus (SADS-CoV) found to be originated from the bat and sparrow respectively causes acute gastroenteritis in the new born piglets ((Wang *et al.*, 2019) [22]. Equine Coronavirus (ECoV), belongs to genus *Betacoronavirus*, found to be associated with the neurological, enteric and pyrogenic disease in equine (Giannitti *et al.*, 2015) [8]. Infectious bronchitis virus (IBV) associated with acute upper respiratory tract infection and nephritis in chicken belongs to the *Coronaviridae* family (Cong *et al.*, 2013) [4]. Even wild aquatic birds are also found to be infected by avian corona virus (Chu *et al.*, 2011) [3]. Also, lab animals like mice and the golden Syrian hamsters can also contract Mouse hepatitis virus (MHV) associated with acute encephalitis and chronic fulminating demyelinating disease and SARS infection respectively (Bender and Weiss, 2010; Roberts *et al.*, 2005) [1, 14].

Damas *et al.*, 2020 [5] conducted a *in silico* scrutiny to know cross species conservation of the ACE-2 receptor in 410 vertebrate including 250 mammals, which supposed to be helpful for the selection of the animal model for COVID-19. As well as, he scored the binding of COVID-19 with ACE-2 receptor as very high, high, medium, low and very low in order to predict susceptible species which can get infected in the Covid-19 pandemic. Further, Binding prediction of SARS-CoV-19 with ACE-2 scored very high via *in-silico* analysis in *Macca Mullatta* and this supported by the finding in naturally infected *Macca Mullatta* in which COVID-19 like symptom developed. However, In some species like Bat, Pangolin (Chinese Pangolin, Manis Pangolin and White bellied Pangoline) low binding score of virus with ACE-2 predicted, where as both horseshoe bat and pangolin is the main suspect supposed to be transmitted infection into the human population. Thus, these findings are indicative of binding of the COVID-19 with the receptor other than the ACE-2.

Bovine CoV (BCoCV) is a pneumoenteric virus which belongs to the *coronaviridae* family of order *Nidovirales*, member of subgroup 2a along with the Swine HEV, CRCoV, Human CoVOC43, HKV-1. HEV causes wasting infection while others causes respiratory and enteric infection in the host. Bovine CoV causes winter dysentery in adults, calf diarrhoea in neonates, and respiratory infection in the all age group of cattle. Subsequently, SARS-CoV known to causes infection in human as well as in the animals like civet cat, raccoon, dog, bat belongs to the subgroup 2b of order *nidovirales*.

Corona virus infections were also reported in the aquatic animals in subsequent studies. Corona Virus belongs to the genus of *Alphacoronavirus*, *Gammacoronavirus*, *Tonovirus*, and *Bafinivirus* has been found infect aquatic organism. In this list, reported corona virus infection in three harbour seals (*Phocavitulina*) which was died due to the acute necrotizing enteritis. Pathological examination of lung further revealed severe diffuse pulmonary congestion as was as focal Broncho alveolar haemorrhages and edema in alveoli. In addition, spleen, peripheral and visceral lymph node showed moderate

to severe lymphoid depletion microscopically. Positive immunofluorescence reaction using the antibody against TGEV, FIPV and CCoV but not with BCCoV (Belongs to betacoronavirus) confirm etiological agents as a alphacoronavirus.

In addition to this, Baluga whale coronavirus SW1 (BWCoV SW1) belongs the genus *gamma coronaviruses* of coronaviridae family was firstly isolated from the captive-born beluga whale which was died due to the liver failure after generalized pulmonary affection. Bottle nose dolphin (BdCoV HKU22) coronavirus was identified in the Indo-Pacific bottlenose dolphins faeces in further studies. Moreover, BdCoV HKU22 causes asymptomatic or mild infection in compression to the BWCoV SW1. In another study, white brim virus (WBV) which belongs to the genus *batinivirus* with in the *nidovirales* order was isolated from the healthy white brim. It was found that WBV closely related with the genus *tonovirus* then other genus of *Nidovirales* order.

Now, the question arises whether veterinarians are required to be alert for the current global pandemic. This question can easily be answered by looking at the outbreak of SARS-CoV-2 which has already been reported in animals. Unlike the previous outbreaks of SARS and MERS, SARS-CoV-2 has already been shown to be acquired by many animal species from human interactions.

#### **SARS-CoV-2 anthroponosis (human-to-animal transmission)**

The first case of contracting the disease from its owner was a pet dog at Hong Kong, China, on 28th February 2020 and fortunately, after taking proper isolation and quarantine measures the dog tested negative to the virus neutralization test conducted on 12 March 2020. The cases reported in animals worldwide are summarized in a table (Table 1).

Results from laboratory experiments concluded that cats are most susceptible to SARS-CoV-2 followed by ferrets, but dogs, pigs and ducks are not. According to OIE, the cats, ferrets and dogs show clinical signs in an order of severe to mild respectively, but there is no observation of any disease symptoms in fruit bats.

After all these spontaneous outbreaks of SARS-CoV-2 in animals, OIE categorized the diseases as one of the “emerging diseases” (OIE, 2020) [11]. In all the above cases, “direct contact” between human and animal has been established as the route of disease transmission.

#### **Broad host range of CoV- factors responsible**

The foremost reason can be that among all RNA viruses, CoV has the highest segmented RNA genome (approx. 30kb), which can be a cause behind its shuffling between numerous host species (Wan *et al.*, 2020) [20].

Among four structural genes of SARS-CoV-2: spike (S), envelope (E), membrane (M) and nucleocapsid gene (N), the first one encodes for spike protein which lies in the receptor binding domain of virus. Spike protein (SRAS-CoV-2 S) is further processed to form a glycoprotein and is expressed on the surface. This glu<sup>394</sup> of spike protein attaches and binds to the lys<sup>31</sup> amino acid of ACE2 receptor (Wan *et al.*, 2020) [20]. Previous studies on 2002-SARS outbreak also concluded that major genetic alterations in the gene responsible for encoding spike protein has transcended the transmission of SARS-CoV from animal to human beings (Song and Park, 2012) [18].

Atomic structural resolution of SRAS-CoV-2 S-ACE2

receptor complex of several species revealed that ACE2 receptor of animals like “pigs, ferrets, cats, and nonhuman primates” are either equally or more susceptible to the receptor binding domain (RBD) of spike protein of SARS-CoV-2 than of human (Wan *et al.*, 2020) [20]. In silico analysis of ACE2 receptor of 410 vertebrates by Damas *et al.* (2020) [5] suggests that SARS-CoV-2 can potentially have a variety of species either as its reservoir or intermediate hosts. Old world primates are at high risk of being susceptible to SARS-CoV-2.

#### **Diagnosis in animals**

In all the confirmed veterinary cases of SARS-CoV-2, the samples collected for examination was vomit, rectal swab, nasal swab or faeces (OIE, 2020) [11]. Since the cases reported were from different developed countries, most of the laboratory confirmation was by real-time reverse transcriptase polymerase chain reaction (RT-PCR) mostly targeting the N-gene of virus and few by next generation sequencing of viral DNA. Centers for Disease Control and Prevention, USA recommends that combination of “fever, coughing, difficulty breathing/shortness of breath, lethargy, sneezing, nasal/ocular discharge, vomiting and diarrhoea” are the symptoms related to infection with SARS-CoV-2 in pets. However, veterinarians should perform extensive differential diagnosis of the patient before recommending for laboratory testing of SARS-CoV-2, as the availability of kits is limited. CDC also directs veterinarians to recommend laboratory testing of animals only after a thorough discussion with state “public health authorities” providing requisite justice to One Health (health of people is connected to the health of animals and our shared environment).

#### **Prevention and Control**

Animal-to-animal and animal-to-human transmission of SARS-CoV-2 is not yet established but few cases of human-to-animal transmission are reported in many countries. Therefore, veterinary staffs either with feverish or other symptoms of COVID-19 should not handle the animal. Nevertheless, in urgent cases of animal handling by a sick veterinarian should follow proper handwashing and face-covering of the personnel to contain the spread of infection. As suggested in the case of humans, only emergency veterinary surgeries should be performed during this period. The government should both legalise and promote veterinary telemedicine facilities in the country as well to reduce the frequency of visiting polyclinics. Contact and epidemiological history of the patient and the owner should be noted down by the staff before treatment. Every government and private veterinary hospital should maintain an isolation room or space to handle both suspected as well as confirmed patients.

It has been found in case of humans that SARS-CoV-2 can spread to different systems like the respiratory, digestive, urinary and haematological system of COVID-19 patient and the virus can be shed to the environment via urine, stool or sputum etc. Therefore, veterinarians should perform an autopsy of either naturally or experimentally infected animals in a thoroughly for examining the dissemination of virus to different organs, which could discover the possible routes of shedding virus by animals. SARS-CoV-2 viruses have been found in feces and vomit samples obtained from infected animals (Table 1). This may raise havoc if any street animal will acquire and start shedding the virus, hence justifying the argument of conducting animal surveillance in the area where

community spread is obvious.

Appropriate steps of putting on and off of personal protective equipment (PPE) should be followed by the veterinarians and staffs while handling the patient. Strict adherence to biosafety and biosecurity should be followed by the veterinarian while treating any patient with infectious disease.

Veterinary surgeons who continue working during the pandemic should remain updated with all the guidelines formulated by the animal husbandry department of their respective countries and also the OIE. It should be the sole responsibility of veterinarians to alert livestock and pet owners at the grassroot level and employees of the zoo.

### Roles and responsibilities of the veterinary profession for public health

Many countries have started imposing lockdown as a preventive measure to tackle the pandemic which resulted in closure of travel, businesses and numerous public services. Concurrently few essential services are still open for the public which also includes veterinary services to keep up the health and welfare of animals. Veterinarians are engaged in the diagnosis, treatment and prevention of diseases in livestock, pets, birds, wild animals etc. in addition to organizing vaccination and deworming camps. On top of that various other crucial roles are still pertaining on behalf of them. Here is a summary of activities where veterinarians can lend their helping hand in fighting COVID-19.

- Veterinary microbiologists and biotechnologists can be recruited in specific laboratories for human sample collection and their screening after undergoing proper training from medical authorities.
- Apart from safeguarding animals by prevention of outbreaks and zoonoses, veterinary epidemiologists can suggest surveillance measures from their experiences from several animal epidemics (avian influenza, rinderpest, bluetongue etc.) occurred in the past, which can ameliorate this disastrous situation (Foddai, Lubroth and Ellis-Iversen, 2020).
- SARS-CoV-2 transmission via food consumption has not been established yet. But amid consumers' fear of acquiring COVID-19 by animal food consumption, proper food processing and inspection is the need of the hour. Heparan sulfate, a negative charged glycosaminoglycan, enriched animal meat is hypothesized to be the eligible anchor for spike protein of SARS-CoV-2 (Pressman *et al.*, 2020). Hence, veterinarians should properly inspect animal food and spread awareness among public against their fear which will be able to possess significant epidemiological implication to ensure safe maintenance of the food chain.
- Management of zoo animals and threatened species by veterinarians necessitates a noteworthy attention.
- As speculated by economists, this pandemic may negatively impact the world economy due to the shutdown of several factories, businesses, construction work etc. Many people lost their jobs temporarily/permanently and have started returning to

their native place. At the grassroot level, veterinarians can be engaged in advising farmers and for raising livestock and managing farms. This can reopen the source of income to the unemployed section and restore the country's economy.

- Ultimate anticipation of the global citizen is the discovery of a vaccine against SARS-CoV-2. Human vaccine development includes various stages of clinical trials which involves animal trials too. Ferrets and hamsters are two animal models, recently suggested by the OIE, for testing of vaccines and drugs against SARS-CoV-2 (OIE, 2020). Beginning with the management of laboratory/experimental animals, developing animal models for virus pathogenesis study to vaccine trials, veterinarians are to be prioritized in all these domains.
- Apart from the above, veterinary researchers can be appointed for human vaccine manufacturing as they have well expertise in the cutting-edge health associated molecular techniques.
- A surge in number of cases of SARS-CoV-2 in animals is well observed and calls for in-depth experiments to develop vaccine for susceptible animals as well.
- Currently many veterinary colleges and research institutes, those are equipped with biosafety level -3 (BSL-3) and real-time PCR machines, are involved in processing and screening human samples for SARS-CoV-2.
- As the world is still not confident to support the fact of animal as the reservoir of SARS-CoV-2, more of the research and surveillance by veterinarians is essential for exploring the accurate source of disease. This can help in building a boundary between the reservoir and human as a measure of prevention of further outbreak.
- Veterinary vaccine manufacturers and pharmaceutical companies can be considered for production of human vaccines and antiviral drugs respectively in huge quantities.
- Veterinary clinics can support the public health response by donating essential materials such as personal protective equipment and ventilators.

### Role of OIE (World Organisation for Animal Health):

- The OIE coordinates with its regional representatives as well as FAO and WHO, to gather information and shares with its members. Rumours and unofficial information are also monitored on day today basis.
- The organization mobilizes several technical working groups ('*ad hoc* groups') to provide scientific advice on research activities and other implications of COVID-19 on animal health.
- The OIE guides veterinary laboratories working with public health services to support testing of human samples for SARS-CoV-2.
- This also works with its Wildlife Working Group and other partners to develop a longer-term plan which objective of understanding the dynamics and risks involved in wildlife trade and consumption.

**Table 1:** list of animals tested positive to SARS-CoV-2

Sl. No	Month of outbreak	Confirmed veterinary case	Place	Clinical signs	Test	References
1	February 2020	Dog	Hong Kong, China	NA	Real-time RT-PCR	OIE
2	March 2020	Dog	Hong Kong, China	NA	Gene sequencing	
3	March 2020	Cat	Belgium	Respiratory symptom	Gene sequencing	

4	April, 2020	Cat	New York, USA	Respiratory symptom	Real-time RT-PCR and gene sequencing
5	April, 2020	Cat	New York, USA	Respiratory symptom	Real-time RT-PCR and gene sequencing
6	May 2020	Cat	France	Respiratory symptom	Real-time RT-PCR
7	April 2020	Mink	Netherland	Gastrointestinal and respiratory symptom	PCR
8	April 2020	Tiger	New York, USA	Dry cough, wheezing and inappetence	Real-time RT-PCR and gene sequencing
9	April 2020	Tiger	New York, USA	Dry cough, wheezing and inappetence	Real-time RT-PCR and gene sequencing
10	April 2020	Lion	New York, USA	Dry cough, wheezing and inappetence	Real-time RT-PCR and gene sequencing
11	May 2020	Cat	Spain	Dyspnoea, tachypnea, thrombocytopenia and hypertrophic cardiomyopathy	Real-time RT-PCR
12	May 2020	Cat	Germany	NA	PCR

### Conclusion and prospects

The origin of SARS-CoV-2 infection in human has not been clearly established yet, however human-to-animal transmission has been well evident in all the reported cases and thus claiming the disease as anthroponosis. Hence there may be a surge in the asymptomatic reservoirs and carriers of the virus that may possibly lessen the chance of limiting the spread of this pandemic. In this scenario many important aspects like food safety, disease diagnosis, prevention of outbreak in human and animals and safeguarding public health etc. play crucial roles in our society. This can only be achieved successfully by including veterinarians in the global health system during this pandemic.

With respect to animal health, companion animals of COVID-19 infected owners should be quarantined and may be recommended for screening for the presence of virus. All zoo keepers should be scanned for the disease before contacting the zoo animals. Army dogs are the most expensive and are also the integral part of the country's security, hence their surveillance is utmost important. Veterinary department of all territories should take the responsibility of reporting the detailed information of all confirmed cases of animals to WOA, OIE within the earliest time. To combat this pandemic, the country's legislation should act vigorously considering the "One Health" approach to conserve the biodiversity by acting synchronously towards welfare of human and animal health combinedly.

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