Exploring human-animal host interactions and emergence of COVID-19: Evolutionary and ecological dynamics

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Abstract

The novel coronavirus disease (COVID-19) that emerged in December 2019 had caused substantial morbidity and mortality at the global level within few months. It affected economies, stopped travel, and isolated individuals and populations around the world. Wildlife, especially bats, serve as reservoirs of coronaviruses from which the variant Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) emerged that causes COVID-19. In this review, we describe the current knowledge on COVID-19 and the significance of wildlife hosts in its emergence. Mammalian and avian coronaviruses have diverse host ranges with distinct lineages of coronaviruses. Recombination and reassortments occur more frequently in mixed-animal markets where diverse viral genotypes intermingle. Human coronaviruses have evolved through gene gains and losses primarily in interfaces where wildlife and humans come in frequent contact. There is a gap in our understanding of bats as reservoirs of coronaviruses and there is a misconception that bats periodically transmit coronaviruses to humans. Future research should investigate bat viral diversity and loads at interfaces between humans and bats. Furthermore, there is an urgent need to evaluate viral strains circulating in mixed animal markets, where the coronaviruses circulated before becoming adapted to humans. We propose and discuss a management intervention plan for COVID-19 and raise questions on the suitability of current containment plans. We anticipate that more virulent coronaviruses could emerge unless proper measures are taken to limit interactions between diverse wildlife and humans in wild animal markets.

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1. Introduction

The recent outbreak of pneumonia in China in December 2019, was caused by a novel Betacoronavirus (2019-nCoV). It was confirmed by deep sequencing analysis of samples taken from lower respiratory tracts of patients (Chen et al., 2020; Huang et al., 2020; Wu et al., 2020a). So far, 2,954,222 (28 April) confirmed cases, 202,597 deaths have been reported in the world (WHO, 2020; Wu et al., 2020a). So far, 2,954,222 (28 April) confirmed cases, 202,597 deaths have been reported in the world (WHO, 2020; Wu et al., 2020a). Therefore, the 2019 novel coronavirus (2019-nCoV) was classified as the SARS-CoV-2 virus name as Severe Acute Respiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS) [Severe Acute Respiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS)] associated with humans (Zhu et al., 2020). Full-genome sequencing and phylogenetic analysis indicated that SARS-CoV-2 is different from the other Betacoronaviruses [Severe Acute Respiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS)] associated with humans (Zhu et al., 2020). Therefore, the novelty of COVID-19 and its swift and sudden onset resulted in the loss of many lives before scientists were able to identify it and establish a preliminary containment plan. In addition, the vast spread of the virus into many countries revealed a serious gap in the biosecurity policies in all countries of the world and consequently shattered the illusion of a stable health security that many developed countries were experiencing.

In recent years, two novel coronaviruses SARS-CoV and MERS-CoV emerged and caused epidemics in 2002 and 2012 worldwide (WHO, 2019, 2003; Wu et al., 2020a). These CoVs were both of zoonotic origin and were transmitted between domestic or captive wild animals and people. Although it was widely suggested that civets were reservoirs of the SARS-CoV, detailed studies revealed that civets likely received the infections from other caged animals (Cui et al., 2019). Less is known about the MERS-CoV that was probably transmitted from bats to dromedaries at least 30 years earlier and continued to circulate within domestic camels, before adapting to humans and emerging as a novel virus in 2012 (Cui et al., 2019). Since Jan 25, 2020, the SARS-CoV-2 global outbreak was unprecedented in recent history, far exceeding the number of cases and deaths (18,398 deaths) in the H1N1 influenza pandemic from 2009 to 2010 (Morens et al., 2010; Viviani et al., 2011).

Wild animal wet markets played a significant role in the COVID-19 outbreak (Cui et al., 2019). It is highlighted broadly in the media and in the scientific literature, that humans became infected with SARS-CoV-2 through contact with animals in Huanan seafood wholesale market (Chen et al., 2020). More importantly, there is mounting evidence that diverse viruses have high frequency of reassortments at the interfaces between human, domestic and wildlife animals (e.g. in live animal markets) (Cui et al., 2019). This has been documented for other pathogenic viruses such as the Highly Pathogenic Avian Influenza H5N1 virus that emerged in 1996 (Takekawa et al., 2010) and coronaviruses such as SARS-CoV that emerged in 2002 (Cui et al., 2019).

To help in evaluating the role of live wild animal markets in the epidemiology of this disease, it is crucial to study this hypothesis critically and to determine the link between viral evolution and mixed animal markets, one of the major human-wild animal interfaces. Our goal here is to shed light on the ecological and evolutionary dynamics relating to the emergence of the SARS-CoV-2. Our brief review on the ecology and evolution of this novel coronavirus and its animal to human transmission, identify gaps in our understanding and highlight management strategies that could be useful in preventing outbreaks in humans, domestic animals and wildlife.

2. Novel human coronaviruses strains and nomenclature

2.1. Coronavirus classification

Coronaviruses (CoVs) are one of the largest positive sense RNA viruses that are about 30 kb in length and that belong to the order Nidovirales, family Coronaviridae, subfamily Coronavirinae. They generally circulate in animals and humans (Fehr and Perlman, 2015; Gorbalenya et al., 2006; Richman et al., 2016). The ICTV currently recognizes four genera of CoVs: Alphacoronavirus (α-CoV), Betacoronavirus (β-CoV), Gammacoronavirus (γ-CoV) and Deltacoronavirus (δ-CoV) (Fan et al., 2019; Paim et al., 2019). Coronaviruses may cause viral diseases in birds and mammals. The Alphacoronavirus and Betacoronavirus mainly infect humans and other mammals and cause diseases especially of respiratory and nervous systems (Tables 1 & 2), whereas Gammacoronavirus and Deltacoronavirus infect birds. Some of the latter two coronaviruses may cause diseases in mammals as well (Table 2) (Cui et al., 2019;
| Virus strain              | Species            | Country  | Taxonomic group | Year | Reference                  |
|--------------------------|--------------------|----------|-----------------|------|----------------------------|
| **Bat viruses**          |                    |          |                 |      |                            |
| Bt-MiCoV-1               | Miniopterus spp.   | China    | I               | 2005 | (Poon et al., 2005)        |
| Bt-CoV-CDPHE15           |                    | USA      | I               | 2006 | (Fan et al., 2019)         |
| Bt-MiCoV-HKU8            | Miniopterus spp.   | China    | I               | 2006 | (Chu et al., 2006; Ge et al., 2016) |
| Bt-PiCoV-HKU5            | Pipistrellus       | Hong Kong| II              | 2006 | (Woo et al., 2006)         |
| Bt-TyCoV-HKU4            | Tylonycteris       | Hong Kong| II              | 2006 | (Woo et al., 2006)         |
| Bt-RoCoV-HKU9            | Rousettus          | China    | II              | 2006 | (Lau et al., 2010; Woo et al., 2007) |
| Bt-Rf-CoV-HuB13          | Rhinolophus ferrumequinum | China | I              | 2015 | (Wu et al., 2016)       |
| Bt-CoV-HKU10             |                    | China    | I               | 2012 | (Lau et al., 2012)        |
| Bt-Rf-CoV-HuB13          |                    | China    | I               | 2012 | (Lau et al., 2012)        |
| Bt-Ny-Sc13               | Nycalus velatimus  | China    | I               | 2016 | (Wu et al., 2016)         |
| Bt-HpCoV-ZJ13            |                    | China    | II              | 2016 | (Wu et al., 2016)         |
| Bt-ScCoV-S12             | Scotophilus spp.   | China    | II              | 2017 | (Lin et al., 2017)        |
| Bt-KYN63                 |                    | Kenya    | I               | 2017 | (Tao et al., 2017)        |
| Bt-CoV-RatG13            | Rhinolophus affinis| China    | II              | 2017 | (Obame et al., 2017)      |
| Bat-CoV-RaTG13           |                    | China    | II              | 2020 | (Zhou et al., 2020)       |
| **Pangolin-CoV**         |                    | China    | I               | 2012 | (Lau et al., 2012)        |
| **Rat viruses**          |                    |          |                 |      |                            |
| MHV                      | Murine             | Czechoslovakia | II           | 1980 | (Bards et al., 1980)      |
| Rt-CoV-LRNV              |                    | Rat      | I               | 2015 | (Wang et al., 2015)       |
| Rt-CoV-HKU24             | Rattus             | China    | II              | 2015 | (Lau et al., 2015)        |
| **Hedgehog virus**       |                    |          |                 |      |                            |
| ErinCoV-1                | Erinaceus europaeus| Germany  | II              | 2014 | (Corman et al., 2014)     |
| **Ferret viruses**       |                    |          |                 |      |                            |
| FRCoV                    | Ferret             | Netherlands | I            | 2011 | (Provacia et al., 2011)   |
| **Mink viruses**         |                    |          |                 |      |                            |
| MCoV                     | Mink               | USA      | I               | 2011 | (Vlasova et al., 2011)    |
| **TGEV**                 | Porcine            | China    | I               | 2013 | (Zhang et al., 2013)      |
| PEDV                     |                    | China    | I               | 2016 | (Xu et al., 2016)         |
| PorCoV-HKU15             |                    | Pig      | IV              | 2017 | (Woo et al., 2017)        |
| **Bovine viruses**       |                    |          |                 |      |                            |
| Bovine coronavirus (BCoV)| Bos taurus         | USA      | II              | 1975 | (Kaye et al., 1975)       |
| BCGO-like coronavirus    | Ovis aries         | Victoria | II              | 1978 | (Tzipori et al., 1978)    |
| BCGO-like coronavirus    | Capra hircus       | Spain    | II              | 1996 | (Munoz et al., 1996)      |
| BCGO                     |                    | Cows     | II              | 2010 | (Woo et al., 2010)        |
| **Feline virus**         |                    |          |                 |      |                            |
| Feline coronavirus       | Cats               | I        | 2010            |      | (Woo et al., 2010)        |
| **Equine virus**         |                    |          |                 |      |                            |
| Equine coronavirus       | Horses             | I        | 2010            |      | (Woo et al., 2010)        |
| **Avian Viruses**        |                    |          |                 |      |                            |
| Influenza, coronavirus   | Gallus gallus     | III      | 2007            |      | (Cavanagh, 2007)          |
| Pigeon coronavirus-IBV   |                    |          |                 |      |                            |
| Duck coronavirus         | Anas platyrhynchos | III      | 2007            |      | (Cavanagh, 2007)          |
| Goose coronavirus        | Anser anser       | III      | 2007            |      | (Cavanagh, 2007)          |
| Turkey coronavirus       | Meleagris gallopavo| III      | 2007            |      | (Cavanagh, 2007)          |
| Pheasant coronavirus     | Phasianus colchicus| III      | 2007            |      | (Cavanagh, 2007)          |
| BuCoV-HKU11              | Bulbul             | Hong Kong| IV              | 2009 | (Woo et al., 2012, 2009)   |
| ThCoV-HKU12              | Thrush             | Hong Kong| IV              | 2009 | (Woo et al., 2012, 2009)   |
| MunCoV-HKU13             | Munia              | Hong Kong| IV              | 2009 | (Woo et al., 2012, 2009)   |
| Wigeon coronavirus       | Anas americana     | Hong Kong| IV              | 2011 | (Chu et al., 2011)        |
| Heron coronavirus        | Ardeo bicuculare/speciosa | Cambodia | IV          | 2011 | (Chu et al., 2011)        |
| Duck coronavirus         | Dendrocygna javanica| Cambodia | III           | 2011 | (Chu et al., 2011)        |
| Duck coronavirus         | Aythya fuligula   | Hong Kong| III              | 2011 | (Chu et al., 2011)        |
| Phalacrocorax corbo     | Phalacrocorax corbo| Hong Kong| IV              | 2011 | (Chu et al., 2011)        |
| Heron coronavirus        | Ardea cinerea     | Hong Kong| IV              | 2011 | (Chu et al., 2011)        |
| Coronavirus              | Anas acuta, Anas penelope, Anas clypeata, Anas crecca| Hong Kong| III & IV | 2011 | (Chu et al., 2011)        |
| WiCoV-HKU18              | Wigeon             | China    | IV              | 2012 | (Woo et al., 2012)        |
| WECoV-HKU16              |                    | China    | IV              | 2012 | (Woo et al., 2012)        |
| SpCoV-HKU17              | Sparrow            | China    | IV              | 2012 | (Woo et al., 2012)        |
| NHCoV-HKU19              | Night heron        | China    | IV              | 2012 | (Woo et al., 2012)        |
Fehr and Perlman, 2015; Perlman and Netland, 2009; Weiss and Leibowitz, 2011; Woo et al., 2012; Yin and Wunderink, 2017).

Most of the HCoV infections are mild although epidemics of SARS-CoV and MERS-CoV (Table 3) in the last two decades collectively resulted in 10,000 cases with mortality rates of 10% and 37% respectively (de Groot et al., 2013; Ksiazek et al., 2003; WHO, 2019, respectively). Prior to the SARS-CoV outbreak, one alphacoronavirus HCoV-229E (which infects humans and bats) and one betacoronavirus HCoV-OC43 (which infects humans and cattle) were known. Both characteristic of illegal wildlife trade. SARS-CoV-2 displayed the structure with the “spike protein” in the membrane envelope (Li, 2017) and this spike glycoprotein (S) from CoV may bind to the host receptors to ease viral entry into target cells and is a primary determinant of cell tropism and pathogenesis (Belouzard et al., 2012; Hantak et al., 2019). There are four amino acid variations of S protein between SARS-CoV-2 and SARS-CoV. SARS-CoV-2 can bind to the ACE2 receptor from the cells from human and other animals (for human-human transmission and cross-species transmission), however, it cannot bind to the cells without ACE2 (Chai et al., 2020; Wan et al., 2020; Zhou et al., 2020). The high affinity between ACE2 and SARS-CoV-2 spike glycoprotein (S) proposed that the people with higher expression of ACE2 might be more vulnerable to SARS-CoV-2 (Guy et al., 2005; Zhao et al., 2020). The trans-membrane protease serine 2 (TMPRSS2) also contributed to the spike glycoprotein (S) priming of SARS-CoV-2, indicating that management of SARS-CoV-2 may be possible through TMPRSS2 inhibitor (Hoffmann et al., 2020; Peng et al., 2020).

### Table 2 (continued)

| Virus strain          | Species                  | Country          | Taxonomic group | Year   | Reference                  |
|-----------------------|--------------------------|------------------|-----------------|--------|----------------------------|
| IBV                   | Poultry birds            | China            | IV              | 2012   | (Woo et al., 2012)         |
| AvCoV–pigeon-67T      | Pigeon                   | Brazil           | III             | 2016   | (Zhao et al., 2016)        |
| AvCoV                 | Anseriformes Columbiformes | Norway         | III             | 2018   | (Martini et al., 2018)    |
| IBV-like              | Anseriformes Charadriiformes | Northern England, Sweden, Poland | III | 2018 | (Milek and Domášiška, 2018) |
| IBV-like              | Anseriformes              | Korea, Madagascar, Beringia, Sweden | III | 2018 | (Milek and Domášiška, 2018) |
| IBV-like              | Passeriformes             | Hong Kong, Cambodia | III & IV     | 2018 | (Milek and Domášiška, 2018) |
| Aquatic animals       | BWCoV-SW1                | USA              | III             | 2008   | (Mihindukulasuriya et al., 2008) |

### Table 3

| Year | Country | HCoV strain | Event description | Fatality rate (%) | Reference                  |
|------|---------|-------------|-------------------|-------------------|----------------------------|
| 2003 | China   | (SARS-CoV)  | very severe pneumonia cases | 10 | (Cheng et al., 2007; Drosten et al., 2003; Ksiazek et al., 2003; Tsang et al., 2003) |
| 2012 | Saudi Arabia | (MERS-CoV) | 1st case of MERS | 37 | (de Groot et al., 2013) |
| 2019 | China   | SARS-CoV-2  | 1st case of COVID-19 | 6.9 | (Chen et al., 2020; Huang et al., 2020; WHO, 2020; Wu et al., 2020) |

3. SARS-CoV-2 genome sequence identity and wildlife

The SARS-CoV-2 caused the deadly infections and spread all over the world at a rapid rate (Chen et al., 2020; Li et al., 2020; Peng et al., 2020; Zhou et al., 2020), so finding the source of SARS-CoV-2 and its main intermediate host is crucial. It is assumed that the SARS-CoV-2 has originated from bats due to its close phylogenetic relationship with beta-genus lineage B bat SARS-CoV (Wan et al., 2020). Angiotensin-converting enzyme 2 (ACE2), the host cell receptor for SARS, has recently been demonstrated in mediating SARS-CoV-2 infection (Chai et al., 2020). Moreover, SARS-CoV-2 probably recognizes ACE2 receptors from a variety of animals such as palm civets (Wan et al., 2020).

The genome nucleotide sequence identity (96.2%) between SARS-CoV-2 and bat CoV (BatCoV RaTG13) in Rhinolophus affinis, indicating that R. affinis bats could be the natural source of the precursors of SARS-CoV-2 (Zhou et al., 2020). However, we may assume that there may be other intermediate hosts for transmission of virus between bats and humans due to differences in sequence identity. Examination of more than 1000 metagenomic samples from pangolins indicated that about 70% contained β CoV (Liu et al., 2019). One coronavirus from the same study had a genomic similarity of 99% with the SARS-CoV-2 genome. This suggested that the pangolin could be a possible intermediate host of SARS-CoV-2 (Wahba et al., 2020). It must be noted here that the pangolins in the study were from smuggling operations, suggesting that the animals were likely held in unhygienic conditions characteristic of illegal wildlife trade. SARS-CoV-2 displayed the structure with the “spike protein” in the membrane envelope (Li, 2017) and this spike glycoprotein (S) from CoV may bind to the host receptors to ease viral entry into target cells and is a primary determinant of cell tropism and pathogenesis (Belouzard et al., 2012; Hantak et al., 2019). There are four amino acid variations of S protein between SARS-CoV-2 and SARS-CoV. SARS-CoV-2 can bind to the ACE2 receptor from the cells from human and other animals (for human-human transmission and cross-species transmission), however, it cannot bind to the cells without ACE2 (Chai et al., 2020; Wan et al., 2020; Zhou et al., 2020). The high affinity between ACE2 and SARS-CoV-2 spike glycoprotein (S) proposed that the people with higher expression of ACE2 might be more vulnerable to SARS-CoV-2 (Guy et al., 2005; Zhao et al., 2020). The trans-membrane protease serine 2 (TMPRSS2) also contributed to the spike glycoprotein (S) priming of SARS-CoV-2, indicating that management of SARS-CoV-2 may be possible through TMPRSS2 inhibitor (Hoffmann et al., 2020; Peng et al., 2020).

4. Evolutionary process: Emergence of novel viruses

Coronaviruses are diverse and are capable of evolving rapidly. Viral emergence may be recognized as a two-step process: (i) introduction of the virus into one of more novel hosts and (ii) adaptation of virus into the novel host species. Rapid evolution of viruses may occur depending on the evolutionary potential of the virus and environmental conditions (Morse, 1991). Knowledge of
the origin of virus is crucial because viruses mutate quickly and unpredictably making viral evolution difficult or impossible to predict (Morse, 1997). This is also the case with SARS-CoV-2. New viruses generally arise from closely related pre-existing viruses. Among emerging infections 75% are zoonotic, originating principally from wildlife (Cunningham, 2005; Daszak et al., 2000). Of the 1415 known human pathogens (including 217 viruses and prions), 61% are zoonotic (Taylor et al., 2001). Most of the major viral disease outbreaks were caused by RNA viruses with higher mutation rates compared to other kinds of microorganisms (Chan et al., 2013; Cheng et al., 2007). HCoVs have long genomes encoding diverse accessory proteins which may stimulate virus adaptation to specific hosts and suppression of immune responses by hosts (Forni et al., 2017). Understanding of evolutionary processes is very important in determining how an existing virus that usually infects animals would be able to cross over into humans (Morse, 1991).

4.1. Natural reservoirs of coronaviruses and their cross-species transmission

Comprehensive investigations are required about the natural zoonotic reservoirs of coronaviruses. It is likely that newly emerging coronaviruses originate from strains circulating in these reservoirs from years. They have the potential of cross-species transmission within domestic or captive, wild animals. Before spillover to humans these coronaviruses most likely adapted to intermediate hosts where there is no direct contact of humans to these natural zoonotic reservoirs. Furthermore, the wild animal wet markets provide enabling conditions for cross-species spillover of these coronaviruses and finally to infect the humans (Bolles et al., 2011).

4.1.1. Coronaviruses transmission from wild animals to humans

Animal coronaviruses have been identified since 1930s and different CoVs have been isolated from various infected animals before the first isolation of HCoV-229E from a patient (Ye et al., 2020). So far, various coronaviruses have been reported in mammalian and avian hosts (Table 2). Most widely studied and of common occurrence are coronaviruses reported in chickens, turkeys, cats, dogs, swine, cattle, mice, rats, rabbits, and humans (Guan et al., 2003; Swayne et al., 2004). The SARS-CoV was detected for the first time in animals during a study conducted in a live animal market (Guan et al., 2003). Viruses closely related to SARS-CoV were found in three different animal species, masked palm civet, raccoon dog and Chinese ferret badger in Shenzhen market, China (Wang et al., 2006). Subsequently, the detection of SARS-CoV infection in humans working at wild animal wet markets where civets were sold proposed that civets perhaps the source of human infections (Wang et al., 2018).

Coronaviruses are found in an exceptionally wide distribution in wild mammals including bats (Table 2) (Lau et al., 2010; Vijgen et al., 2005). Compared to human coronaviruses, the genetic diversity of bat coronaviruses is so huge that it is speculated that bats are the hosts of all mammalian coronaviruses (Drexler et al., 2010; Vijaykrishna et al., 2007) and this huge genetic diversity offers a chance for the emergence of novel animal and human coronaviruses. The occurrence of highly pathogenic coronaviruses such as SARS-CoV, MERS-CoV and severe acute diarrhea syndrome coronavirus (SADS-CoV) which shattered the livestock industry by infecting pigs (Zhou et al., 2018) were caused by coronaviruses of bat origin. Thus, the next viral disease events may be due to bats coronaviruses, changing ecological and epidemiological situations. Three HCoVs outbreaks (Table 3) including COVID-19 leading us that there is urgent need to study the reasons of coronaviruses emergence to avoid future outbreaks. Out of thirty eight, twenty two bat-borne viruses are found in China (Fan et al., 2019). Consequently, due to Chinese food culture (Fan et al., 2019) it is assumed that bat-borne CoVs can re-emerge and hotspot of next disease outbreak may be China.

The natural recombination between distantly related African bats (Triaenops afer and Hipposideros sp.) CoVs created NL63-like virus perhaps responsible for HCoV-NL63. Consequently, the interspecies recombination may perhaps contribute in CoVs evolution and emergence of novel coronaviruses with zoonotic potential with different genotypes for instance three genotypes in HCoV-HKU1 (Tao et al., 2017). In one longitudinal study of bat coronaviruses in a cave system from Yunan China, researchers found all known SARS-like coronaviruses (SARSr-CoVs) over a five year period (Cui et al., 2019). However, the direct progenitors of SARS-CoV have never been isolated from wild bats, suggesting that recombination can be occurring elsewhere. As of now, a lot of the evidence points towards wild animal wet markets where many species of animals ranging from mammals to fish are sold. These markets have been important in reassortments of other types of viruses (e.g. well documented in the emergence of highly pathogenic avian influenza H5N1 subtype in mixed poultry markets) (Takekawa et al., 2010). Since, wild animal markets are not well studied; there must be a concerted effort to study existing CoV diversity and their variants in wild animal markets.

Furthermore, a wide variety of CoVs have been observed in birds (Table 2). However, birds are infected by Gamma and Delta-coronaviruses that are not adapted to mammalian hosts (Cui et al., 2019). Thus, birds can be precluded as possible hosts of progenitors of coronaviruses of human importance. Additionally molecular epidemiological research studies in bats, civets, pangolins or other forest mammals and birds, and complete genome sequencing will contribute to know the CoVs diversity and their evolutionary processes and histories to protect global health (Woo et al., 2009).

It is crucial to recognize animals that are susceptible to these coronaviruses as there are vast numbers of live animals kept and sold in wild animal wet markets (Wang et al., 2006). In the past, more than 10 mammalian species were proven susceptible to the SARS-CoV or related viral infections (Wang et al., 2006) including rats. Rats were involved in the spread of SARS-CoV during SARS outbreaks in Hong Kong (Ng, 2003), however, further studies are required to elucidate their potential role in CoVs transmission. Domestic poultry were excluded as reservoirs or linked with the spreading of SARS-CoV in the animal markets because avian species were not susceptible to SARS-CoV infection (Swayne et al., 2004; Weingartl et al., 2004).

Diverse groups of wild animals are collected in wild animal wet markets across Asia, particularly southeastern and eastern Asia often transported over large distances and crammed together into cages. These animals are stressed and immunosuppressed and shed infective stages of pathogens from existing infections, while also being increasingly vulnerable to new infections from within the wet market system (Cunningham, 2020). Co-infection of more than one variant of a given virus increases the chances of reassembly of viruses that leads to the emergence of novel genotypes (Cunningham, 2020; Takekawa et al., 2010)(Fig. 1). The extent to which this has happened in coronaviruses is not clear, but this must have happened before the CoVs could adapt to other mammals in the wild animal wet market systems. Subsequent to this, the likely exposure of humans in the wild animal wet markets allowed the novel genotypes of CoVs to make the ‘jump’ and adapt to humans (Cui et al., 2019) like SARS-CoV-2.

4.1.2. History of interspecies transmission of HCoVs

Human coronaviruses (Table 1) have a strong history of interspecies transmission and are of zoonotic animal origin (Rest and
Mindell, 2003). HCoVs including SARS, MERS, OC43, 229E and new SARS-CoV-2 all evolved through likely host shifts from animals to humans and created coronavirus disease epidemics and pandemics. It is evident that OC43 had a high sequence similarity with bovine Betacoronavirus (BCoV) whereas 229E probably emerged from a bat Alphacoronavirus (Bolles et al., 2011; Kocherhans et al., 2001). However, investigations are still needed to confirm the origins of HCoV-NL63 and HCoV-HKU1. SARS, MERS and novel SARS-CoV-2 most likely have bat origin (Bolles et al., 2011; Song et al., 2005).

5. Anthropogenic factors that affect emergence

Ecological changes due to agricultural or economic development are among the most common known factors governing the emergence of novel viruses and their outbreak. Climate change deforestation and industrialization are main factors that are changing the habitats of wildlife and consequently permitting the displacement and mixing of various hosts that harbor coronaviruses and other pathogens (Chan et al., 2013). Urbanization poses significant threats to the ecology and population dynamics of animals in different natural ecosystems. Through urbanization, humans are encroaching further into the natural habitats of animals and creating overlapping areas where there are more chances of exchange of diseases between humans and wildlife. Humans are responsible for spreading pathogens into new areas or new populations through the travel and trade (Wu et al., 2017). Through the advances in travel and transportation technology, we are now globally connected and trading in distant regions to boost economies and consequently spreading viruses, vectors and hosts in distant regions (Wu et al., 2017). Through these different factors we are enhancing the intermingling of diverse viral genotypes in various host populations which affect the genetic make-up and immune responses of host populations. Ultimately, greater exposure to novel pathogens could lead to emergence and re-emergence of diseases sometimes in disparate geographic regions (Xu et al., 2012).

Human coronaviruses SARS-CoV, MERS-CoV and now the novel SARS-CoV-2 which is the cause of COVID-19 pandemic is believed to have originated in wild animals and bats are most likely the natural reservoir of these viruses (Forni et al., 2017). Due to current menace and future threats of viral diseases scientist are now more interested in the ecology and evolution of coronaviruses (Graham et al., 2013) to see the sink and sources in life cycle of coronaviruses for their management options and to stave off coronaviruses spillover in human populations.

Coronaviruses spread from bats to humans involves some conditions for instance dispersion of reservoir hosts, viral contamination of the hosts, exposure of recipient host to reservoir and susceptibility of recipient hosts. The overlapping areas of reservoir and recipient hosts describes the probable zones of high risk of transmission and infections of viruses in recipient hosts (Plowright et al., 2014), and this was the case in outbreak of novel coronavirus SARS-CoV-2 in live animal market of Wuhan, China, where live wild animals of all kinds including bats, pangolin and palm civets were on sale (Plowright et al., 2014).

6. Management of coronaviruses outbreaks

Little is known of the epidemiology of human infections with coronaviruses. Here, we propose management intervention in five major areas: i) mitigating or banning wildlife trade to avoid the exposure of coronaviruses to new hosts and new places ii) overlapping areas between domestic animals and wildlife due to deforestation and urbanization iii) managing or closing the wild animal wet markets where vast variety of wild and domestic animals are on sale which provide ideal condition for viruses reassortments and evolution of novel coronaviruses iv) managing livestock which may reduce the probability of exposure to viral diseases v) control strategies to reduce the chances of viruses spillover from animals to humans.

Moreover, investigations and continuous surveillance for new coronavirus pathogens in natural ecosystems, overlapping areas of wildlife and livestock, and especially in wild animal wet markets are necessary to stave off the concurrence of new viruses’ evolution and emergence and their spill over to humans.

7. Conclusion

Since the history of two HCoVs pandemics (SARS-CoV and MERS-CoV), many evidences showed that both have a bat origin.
and are spread to humans via intermediate hosts. Coronavirus originating in bats most likely spilled over into wild animal wet markets where variant circulated and reasserted to produce the SARS-CoV-2 virus. Consequently, the role of intermediate hosts is very important to understand mechanisms of spillover and subsequent adaptation of viruses to humans. At present, COVID-19 has been spread worldwide. Conditions that increase the interactions at the interface between humans and wildlife such as wet markets exist throughout Southeast Asia, including China, constituting a risk for the emergence of novel coronaviruses. Determining transmission routes between wildlife and humans is a challenge and new molecular techniques are instrumental in improving our understanding emerging infectious diseases of significance to human’s health, domestic animal and wildlife. We suggest that the most effective way to prevent emergence of novel coronaviruses (or other viruses) is through a total ban of wildlife trade, since contact between diverse viruses occur at these interfaces.

COVID-19 needs to be studied intensely as this is a global health threat. Careful surveillance is crucial due to the pandemic potential of SARS-CoV-2, to monitor future host adaptions, especially in wild animal wet markets and associated wildlife trade, since contact between diverse viruses occur at these interfaces. Viruses are spread to humans via intermediate hosts. Coronaviruses (or other viruses) is through a total ban of wildlife trade, since contact between diverse viruses occur at these interfaces. Pasteurization of and sale of bats in such markets were dedicated for combating non-communicable diseases such as cancer, which claim a predictable number of lives via a predictable trend. But, after COVID-19, more money and research should be devoted to study unpredictable emerging pandemic diseases. As a result, inter-country research grants should be made available to research teams worldwide.

COVID-19 destroyed the fake sense of biosecurity, which was established in many countries in the past century. Consequently, this should trigger a comprehensive review process of the current health systems and emergency plans.

8. Learned lessons and recommendations

There is a gap in the research conducted on bats and a host of forest mammals, as reservoirs or intermediate hosts of coronaviruses. Future research should investigate viral loads, genetic variation and potential for reassortments, especially in countries where there is direct contact between humans and bats. It is clear that big funds and large number of studies were dedicated for combating non-communicable diseases such as cancer, which claim a predictable number of lives via a predictable trend. But, after COVID-19, more money and research should be devoted to study unpredictable emerging pandemic diseases. As a result, inter-country research grants should be made available to research teams worldwide.

COVID-19 destroyed the fake sense of biosecurity, which was established in many countries in the past century. Consequently, this should trigger a comprehensive review process of the current health systems and emergency plans.

Ethical approval

Ethical approval is not required.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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