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HISTORY OF EPIZOOTICS, EPIDEMICS AND EVOLUTION OF CORONAVIRUSES

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1. ABSTRACT

As emerging coronaviruses have always become a global human and animal health problem, especially SARS-CoV, MERS-CoV and SARS-CoV2 (severe acute respiratory syndrome coronavirus 2), many researchers have focused on the epidemic, virological and clinical characteristics of each coronavirus since the first description of IBV (infectious bronchitis virus) in 1930. Unquestionably, bats act as a natural reservoir for many viruses, including coronaviruses, and have played a crucial epidemiological role in the emergence of many viral diseases in humans or animals via other animals as intermediate hosts. In this review, we will try to situate the different epizootics and epidemics caused by CoV, their reservoir as well as their evolution in relation to the history of human intrusion on their environment.

Keywords : *Coronavirus, bats, tMRCA; viral evolution, animal host, intermediate host.*

2. INTRODUCTION

Coronaviruses (CoV) are enveloped riboviruses, grouping many viruses that infect several animal species (avian and mammalian), including humans. The term "coronavirus" appeared only in 1968 after the identification of the first human CoV or HCoV (Almeida J. D et al., 1968). The authors compare this type of virus spherical, with rounded excrescences, formed mainly by the spike (S) and protein that resembles a petal with its crowns or "*corona*" in Latin (Figure-1).

Figure 1: Schematic structure of coronavirus. The virus is an enveloped, non-segmented, positive-sense single-stranded RNA virus. The virion has a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid (N) protein, which is buried inside phospholipid bilayers and covered by the spike glycoprotein trimmer (S). The membrane (M) protein hemagglutinin-esterase (HE) and the envelope (E) protein are located among the S proteins in the virus envelope (Jafari A et al., 2020).

Coronavirus genomes (27-33 kb) encode five large open reading frames (ORFs), including one polyprotein (ORF1a/ORF1ab) in the 5' and four structural proteins in the 3', namely spike (S), envelope

(E), membrane (M), and nucleocapsid (N) proteins (Figure-xx), common to all CoVs (Ashour et al., 2020). Yet, some CoVs possess a fifth structural protein called HE or hemagglutinin-esterase (Fehr and Perlman, 2015). In addition to these structural proteins, CoVs also have accessory proteins that interpose between the structural proteins and vary from each CoV (Figures-2).

Figure 2: 3' side of the SARS-CoV, MERS-CoV and SARS-CoV2 genomes showing structural and accessory proteins. Adapted according to Shah's team in 2020 ((Shah et al., 2020).

After the release of the CoV genome into the host cell cytoplasm upon entry marks the beginning of a complex viral gene expression program, which is highly regulated in space and time (V'kovski et al., 2021). Translation of ORF1a and ORF1b from genomic RNA produces two polyproteins, pp1a and pp1ab, respectively. Sixteen nonstructural proteins (nsp) are released upon proteolytic self-cleavage by the two cysteine proteases located in nsp3 for papain-like protease (PLpro) and nsp5 for 3CLpro or chymotrypsin-like protease (Figure-3).

Figure 3: The 16 nsp of SARS-CoV2 according to V'kovski's team in 2021 (V'kovski et al., 2021)

3. HISTORY OF DISEASES CAUSED BY CORONAVIRUSES

The first strain of CoV, IBV or *Infectious Bronchitis virus* (Figure 4), was isolated and identified from infectious bronchitis in chickens in the 1930s (Beaudette and Hudson, 1937). In human medicine,

research on HCoV did not really start until the identification of the SARS-CoV strain in China in 2003 (Peiris et al., 2004), except for a few authors who reported the first human CoVs *HCoV-229E* and *HCoV-O43*, which cause common colds in humans (Bradburne, 1970; Hamre and Procknow, 1966). Prior to 2003, the majority of published articles on CoVs refer only to epizootics in livestock (Chasey and Cartwright, 1978; Dea et al., 1981; Doyle and Hutchings, 1946; Tobler and Ackermann, 1996), companion animals (Herrewegh et al., 1998) and mice (Bailey et al., 1949).

Figure 4: Chronological representation of CoV epizootics and epidemics (Maminaiina OF et al., 2020)

3.1. CoV diseases in animals

3.1.1. Avian infectious bronchitis with coronavirus or CoV-IBV

The first strain of CoV-IBV, is the agent of avian infectious bronchitis of the genera *Gallus gallus domesticus* (chickens) and *Anser anser* (geese) (Beaudette and Hudson, 1937; Cavanagh and Gelb, 2008; Pauly et al., 2019). Infection is characterized by acute respiratory distress, rales, coughing, nephritis, severe clutch drop, deterioration of egg quality, and high mortality in young chicks (Bande et al., 2016).

3.1.2. Porcine hemagglutinating encephalomyelitis or PHE

PHE-CoV, the causative agent of neurological and/or digestive diseases in pigs (Mora-Díaz et al., 2019), was one of the first porcine CoVs identified in 1957 and the only neurotropic CoV affecting pigs (Mora-Díaz et al., 2019; Roe and Alexander, 1958). Clinical manifestations, including vomiting and emaciation and/or neurological signs, are age-related and are typically reported only in piglets less than 4 weeks of age. Subclinical circulation of *PHE-CoV* has been reported worldwide (Mora-Díaz et al., 2019). *PHE-CoV* and some other *BetaCoV* have a second, shorter spicule, the hemagglutinin-esterase or HE protein (Zeng et al., 2008).

3.1.3. Porcine Epidemic Diarrhea or PED

PED-CoV was determined to be the etiologic agent of porcine epidemic diarrhea in the late 1970s (Lee, 2015; Pensaert and de Bouck, 1978). Since then, the disease has been reported in Europe and Asia

(Antas and Woźniakowski, 2019; Brnić et al., 2019; Hanke et al., 2017; Song et al., 2015). PED-CoV causes acute diarrhea, vomiting, dehydration, high mortality in suckling piglets and severe gastroenteritis in young piglets (Antas and Woźniakowski, 2019). PED-CoV presents a similar clinical picture with TGE-CoV and PD-CoV (Chen et al., 2019). In addition, coinfection can occur (Marthaler et al., 2014).

3.1.4. Transmissible swine gastroenteritis or TGE

TGE-CoV, which causes *porcine transmissible gastroenteritis*, was identified in the United States in 1945 (Doyle and Hutchings, 1946). Subsequently, the disease has been reported in many countries in Europe, Asia, Latin America and Africa (Cubero et al., 1993; Falsey et al., 1997; Hou et al., 2012; Martins et al., 2013; McIntosh, 1974; Pyrc et al., 2010; Williams et al., 1994). TGE manifests as an epidemic of watery diarrhea with vomiting, rapidly spreading affecting virtually all pigs in contact within days (Aynaud et al., 1985; Haelterman and Hooper, 1967). This *enteropathogenic TGE-CoV*, affects pigs of all ages (Martins et al., 2013).

3.1.5. Porcine Respiratory CoV or PR-CoV

PR-CoV was first identified in Belgium in 1984 (Usami et al., 2008) and subsequently in several countries including China, Japan, Uganda, and the United States (Laude et al., 1993; Muley, 2012; Wang et al., 2014). This CoV has a close antigenic relationship with enteropathogenic PEG-CoV (Rasschaert et al., 1990).

PR-CoV, derived from TGE-CoV by deletion of part of the S gene, has lost its tropism for enterocytes and increased its tropism for the respiratory tract. It can cause mild respiratory disease in pigs, although most infections are subclinical (Chen et al., 2019). These two CoVs are cross-reactive, but serological tests are available to distinguish between them (Chen et al., 2019).

3.1.6. Porcine Deltacoronavirus or PD

Initially, PD-CoV was detected in 2009 in porcine fecal samples in Asia and then pigs in Hong Kong in 2012 (Woo et al., 2012). This CoV was not identified until 2014, when it caused diarrhea in pigs in the United States (Lee, 2015; Woo et al., 2012; Zhang, 2016; Zhou et al., 2018). Of unknown origin, genomic analyses suspect that PD-CoV may originate from an ancestral avian *DeltaCoV (DCoV)* (Woo et al., 2012). PD-CoV has caused diarrhea and intestinal lesions in infected piglets (Jung et al., 2015; Vitosh-Sillman et al., 2016). PD-CoV continues to circulate and cause disease in swine herds worldwide (Boley et al., 2020).

3.1.7. Swine Acute Diarrhea Syndrome or SADS

In 2017, a fatal piglet diarrhea occurred in Guangdong Province, China (Zhou et al., 2019). This is Swine Acute Diarrhea Syndrome due to *Swine Acute Diarrhea Syndrome-CoV* or SADS-CoV (Gong et al., 2017; Pan et al., 2017). SADS-CoV is related to HKU2 virus found in bats of the genus *Rhinolophus* which is

also shown to be the source of SARS-CoV from 2002-2003 (Cui et al., 2019). Since then, the disease has been controlled by immunizing sows from the intestines of infected piglets, but re-emerged on a pig farm two years later (Zhou et al., 2019). Apart from diarrhea, the disease also causes vomiting and weight loss in piglets which results in considerable economic loss in pig industry (Gong et al., 2017; Pan et al., 2017; Zhou et al., 2018). The mortality rate reaches 90% (Zhou et al., 2018).

3.1.8. *Diarrhea, dysentery and respiratory infections in cattle*

Bovine CoV or BCoV causes three different diseases in cattle, as well as goats and sheep: calf diarrhea, winter dysentery, and respiratory infections such as bovine respiratory disease complex known as "*shipping fever*" in fattening (Balasuriya et al., 2017; Caswell and Williams, 2016; Peek et al., 2018; Underwood et al., 2015) and dairy producing animals (Perlman and Netland, 2009). The virus causes heavy economic impact in beef industry (Balasuriya et al., 2017). The form and severity of BCoV disease is related to season, age of animals, and secondary infections (Balasuriya et al., 2017).

In calves, BCoV diarrhea is often associated with other pathogens, *Rotavirus* and *Cryptosporidium*. A severe form is observed in case of co-infection with *Bovine Viral Diarrhea Virus* (BVDV), a *Pestivirus* of the family *Flaviviridae* (Uzal et al., 2016).

In winter, dysentery occurs in adult animals with a sporadic pattern (Balasuriya et al., 2017). Signs appear 20-36 hours after infection (Underwood et al., 2015).

In addition to the two digestive diseases, BCoV also causes mild respiratory signs such as cough and rhinitis or severe signs such as pneumonia in calves 2-6 months of age (Balasuriya et al., 2017). Healthy or diseased carrier cattle then excrete BCoV either through the respiratory or digestive tract (Balasuriya et al., 2017).

3.1.9. *Feline CoV Complex*

Feline CoV or FCoV causes a mild or asymptomatic infection in domestic cats (Myrrha et al., 2011). But, persistent infection can cause the virus to mutate into a highly virulent strain called *Feline Infectious Peritonitis CoV* or FIP-CoV. This virulent strain, FIP-CoV is the cause of feline infectious peritonitis. FIP was discovered in 1963 in the United States (Holzworth, 1963) but FCoV was discovered only a few years later (Ward, 1970). Based on their variability, antigenicity, and *in vitro* growth pattern, FCoV can be divided into two serotypes: FCoV types-I and II (Fiscus and Teramoto, 1987; Shiba et al., 2007). The FCoV *type-II* variant is the result of heterologous recombination between the canine CoV variant CCoV *type II* and the feline FCoV *type-I* variant (Buonavoglia et al., 2006).

3.1.10. *Canine CoV Complex*

The first canine CoV or CCoV infection was reported in 1971 (Binn et al., 1974). Through molecular biology and pathobiology, much has been learned about CCoV. Like FCoV, CCoV is subdivided into two serotypes: CCoV *type-I* and CCoV *type-II* (Pratelli, 2006). CCoV *type-I* is genetically more similar to FCoV

type-I than to *CCoV type-II* (Pratelli et al., 2003). Indeed, they evolved from a common ancestral virus (Licitra et al., 2014). *CCoV type I* infection in dogs is restricted to the enteric tract (Buonavoglia et al., 2006) and produces only mild or asymptomatic forms (Tennant et al., 1991). Whereas *CCoV type-II* is a *pantropic* variant that is highly pathogenic to dogs (Buonavoglia et al., 2006).

3.2. CoV diseases in humans

After the discovery of the first strain of human CoV or HCoV, epidemiological studies have shown that CoV are generally associated with mild respiratory infections. *HCoV-associated* pathologies were not considered sufficiently moderate and did not arouse a clear interest in researchers. Thus, complete genomic studies of HCoV were not performed until 2003, following the identification of SARS-CoV, the infectious agent responsible for Severe Acute Respiratory Syndrome in China. Since then, three fatal HCoV outbreaks have been reported in 2002, 2012, and recently in 2019 (Figure 4). The severity of the infections varies from outbreak to outbreak although their clinical features are similar to themselves and other respiratory infections, making diagnosis difficult (Wang et al., 2020b).

3.2.1. Cold flu

CoVs are among the infectious agents that cause the common cold in humans during the winter months (Birch et al., 2005; Davis et al., 2018; Falsey et al., 2002; Tyrrell and Bynoe, 1965; van der Hoek et al., 2004). The first two strains of HCoV (*HCoV-229E* and *HCoV-OC43*) were isolated in 1962 and 1967, respectively (Bradburne et al., 1967; Hamre and Procknow, 1966; McIntosh et al., 1967; Woo et al., 2005). After the SARS event in China, two other HCoV strains (*HCoV-NL63 in 2004* and *HCoV-HKU1 in 2008*) were isolated from patients with bronchiolitis and viral pneumonia (Cui et al., 2011; Lau et al., 2006; van der Hoek et al., 2004; Woo et al., 2005).

These four HCoVs are endemic and cause 15-30% of upper respiratory tract infections each year (Fehr and Perlman, 2015; Jonsdottir and Dijkman, 2016; Larson et al., 1980). In addition, these HCoVs are adapted, spread and co-circulated in the human population (Kim et al., 2016).

3.2.2. Severe Acute Respiratory Syndrome (SARS-2002)

In 2002-2003, severe acute respiratory syndrome (SARS) emerged in Guangdong Province, China (Fields et al., 2013; Zhong et al., 2003). The disease clinically manifests as fever, headache, rhinorrhea, dry cough, difficulty breathing (Burrell et al., 2017; Cherry, 2004) and can progress to fatal pneumonia (Cherry, 2004). SARS-CoV infection has resulted in 8,096 cases and 774 deaths (Cherry, 2004) with 66% of cases in China and has spread to 36 countries (Cherry, 2004; Swerdlow and Finelli, 2020). The overall mortality rate is 9.6-15% while the reproduction rate is greater than 2 (Swerdlow and Finelli, 2020). SARS-CoV is considered extinct within two years of its occurrence (Bleibtreu et al., 2019).

3.2.3. Middle East Respiratory Syndrome (MERS)

In June 2012, a new respiratory syndrome was detected in Saudi Arabia (Bleibtreu et al., 2019; Burrell et al., 2017). The outbreak spread to 27 other countries (Bleibtreu et al., 2019; Burrell et al., 2017). After incubation, the most common symptoms are influenza-like illness (Mohd et al., 2016). The disease can be accompanied by acute respiratory distress syndrome, severe pneumonia, and multiple organ dysfunction resulting in death of the patient (Arabi et al., 2014; Garbati et al., 2016; Joob and Wiwanitkit, 2016; Mohd et al., 2016). To date, the majority of cases have been reported from Saudi Arabia (Bleibtreu et al., 2019).

3.2.4. Wuhan pneumonia or COVID-19

In late 2019, a new, unknown human CoV was identified in the city of Wuhan, China (Chan et al., 2020; Wang et al., 2020b; Wu et al., 2020b). In 2018, WHO already predicted a future deadly respiratory "disease X" (Honigsbaum, 2019). This disease is the third human CoV epidemic called COVID-19 or CoV Disease 2019 whose causative agent is SARS-CoV2 (Lai et al., 2020), formerly known as 2019-nCoV (Paraskevis et al., 2020; Tang et al., 2020a; Wang et al., 2020a). Since its discovery, the number of reported cases of COVID -19 has been steadily increasing in several countries and WHO has classified it as an epidemic and then a pandemic of COVID -19 (World Health Organization, 2020).

4. ORIGIN AND EVOLUTION OF COV

4.1. Evolution and plasticity of CoV

The significant plasticity of their genome makes CoVs agents with high evolutionary potential (Karamitros et al., 2020). The two major modes of CoV evolution are mutations and recombination (Wu et al., 2020a). Indeed, recombination was concluded by Forni's team in 2017 to explain the origin of ORF8 of SARS-CoV, which has high sequence identity with that of civet CoV (Forni et al., 2017). The acquisition of an ORF8 (accessory protein) closely related to that of civet/human SARS-CoV was the results of recombination between CoVs within SARSr-Rs-CoV (*Rs: Rhinolophus sinicus*) or between SARSr-Rs-CoV and SARSr-Rf-CoV (*Rf: Rhinolophus ferrumequinum*) from bats (Lau et al., 2015b; Wu et al., 2016).

In CoV, despite the presence of nsp14 proofreading function (Ma et al., 2015), the replication complex generates many variants (Becares et al., 2016; Snijder et al., 2003). As with all RNA viruses, CoV is heterogeneous and has a quasi-species distribution (Mandary et al., 2019). This distribution can be seen as an optimization strategy to cope with environmental changes (Vignuzzi et al., 2006). It has been described for several CoVs not only in persistent infections, but also in acute infections (Lin et al., 2020; Mandary et al., 2019; Tang et al., 2020b).

In bats, various CoVs are zoonotic potentials. Indeed, there are many opportunities for these zoonotic CoVs to evolve and recombine, leading to the emergence of new CoVs that are in the future more transmissible and/or lethal, in domestic animals as well as in humans (Ye et al., 2020).

4.2. Reservoirs of CoV

Birds and bats are the primary reservoirs of CoV (Woo et al., 2012). Due to their clustering behavior and ability to fly long distances (Chan et al., 2013; de Sales Lima et al., 2015), they have the potential to spread emerging viruses among themselves and to other animal species and humans (Woo et al., 2012). Indeed, the flight adaptation of bats and birds promotes a rise in their body temperature allowing for an increased efficiency of the immune response (O'Shea et al., 2014; Rodhain, 2015; Zhang et al., 2013).

Bats harbor a diversity of CoVs including the ancestors of *AlphaCoV* and *BetaCoV* (Vijaykrishna et al., 2007), while the CoVs of birds are the ancestors of *GammaCoV* and *DeltaCoV* (Figure 5).

Figure 5: Evolution of CoVs from their ancestors in bats, birds and rodents to virus species that infect other animals. Dashed arrows, possible transmission routes from bats or birds to rodents before the establishment of the A lineage. *Betacoronavirus* (Woo et al., 2012)

4.3. Origin of the CoV

Phylogenetic dating on RNA-dependent RNA polymerase divergence (nsp12:RdRp) suggests that the time of the most recent common ancestor or tMRCA (*Time of Most Recent Common Ancestor*) of mammalian *AlphaCoV*, *BetaCoV* and avian *GammCoV* appeared around 7,000 - 8,000 BP or Before Present (Figure 6). That of *GammaCoV* and *BetaCoV* with *DeltaCoV* goes back another 2,000 years earlier to around -10,000 BP (Chan et al., 2013). These dates coincide with the onset of various human agricultural activities during the Neolithic Revolution (Figure-7) such as forest clearing for agriculture and domestication of wild animals (Borrell et al., 2015; Richards, 2002). These activities have led to a significant change in the ecology and population dynamics of CoV, due to the intrusion of wildlife habitat and the intensified mixing of wild or domestic animals, as primary, secondary, or tertiary hosts

(Chan et al., 2013; Jones et al., 2013). Clearly, these human activities increase the potential for transmission of infections between bats, either with domesticated animals or with humans, via these intermediate hosts (Woo et al., 2012).

Figure 6: Molecular dating estimating the divergence of the genera AlphaCoV, BetaCoV, GammaCoV and DeltaCoV. This tree was generated by analyzing the RNA-dependent RNA polymerase (RdRp) genes under the relaxed clock model with an uncorrelated logarithmic normal with BEAST software. The values at the branch points represent the estimated time divergence in number of years to the present according to Woo's team (Woo et al., 2009).

Figure 7: Neolithic Revolution - locations and dates of domestication of major domestic animals (Larson and Fuller, 2014)

For years prior to the SARS outbreak in 2003, CoVs have been identified to cause various diseases in companion and production animals, often requiring vaccination (Gerdtz and Zakhartchouk, 2017; Takamura et al., 2002). For the case of viruses causing infectious bronchitis (*IBV* - *GammaCoV*) in chickens, tMRCA with *Alpha* and *BetaCoV* has been traced back to around 8,000 BP (Figure-xx). *IBV* was first described in 1937 (Cook et al., 2012) phylogenetically very similar strains have been found in several wild bird species (de Sales Lima et al., 2015; Hughes et al., 2009). In Madagascar, 28% (Lac Alaotra - n=357) of individuals tested (17 wild bird species) tested positive for *GammaCoV* and the species *Foudia madagascariensis*, with a rate of 27% (n=11), was the most prevalent (de Sales Lima et al., 2015). The presence of different *GammaCoV* species in several healthy wild bird species (de Sales Lima et al., 2015; Liu et al., 2005; Sun et al., 2007), demonstrated the circulation and adaptation as well as evolution of *GammaCoV* in poultry (Hughes et al., 2009). In other words, the presumed intermediate hosts of this avian *IBV CoV* are wild birds (Mohammed et al., 2019). Since then, this avian disease has resulted in highly contagious and deadly acute respiratory epizootics worldwide (Cavanagh, 2007). Like other CoVs and *Riboviruses*, *GammaCoVs* are characterized by high genetic diversity induced by mutation and recombination (McKinley et al., 2011; Moreno et al., 2017). In addition, the massive vaccination campaign has generated positive selection at the spike or S glycoprotein level of circulating *IBV* strains (Franzo et al., 2019; McKinley et al., 2008). These characteristics can lead to the emergence of new *GammaCoV* and new lethal epizootics in avian species at any time (Woo et al., 2009).

In humans, intermediate hosts, such as cattle (Bovidae: *Bos sp*), alpaca (Camelidae: *Vicugna pacos*), dromedary (Camelidae: *Camelus dromedarius*), rodents (*Rattus sp*), and palm civet (Viviveridae: *Paradoxurus hermaphroditus*), have been cited as the origin of viruses, *HCoV-OC43* (Hayman et al., 2013), *HCoV-229E* (Pfefferle et al., 2009), *MERS-CoV* (Zaki et al., 2012), *HCoV-HKU1* (Lau et al., 2015a) and *SARS-CoV1* (Drosten et al., 2003).

Indeed, the *HCoVs* responsible for the winter cold (*-229E*, *-OC43*, *-NL63*, and *-HKU1*) are currently well-adapted after hundreds or thousands of years of circulation in the human population. Their evolutionary histories and associations with its hosts provide important information about the history of winter cold epidemics (Corman et al., 2018; Kim et al., 2016). The probable tMRCA of these four winter cold-causing *HCoVs* are found in the years 1,200-1,500 ; 1,800 ; 1,900 and 1,950 respectively (Forni et al., 2017; Lau et al., 2015a; Pfefferle et al., 2009). These dates coincided respectively with European discoveries of new lands such as America in the year 1500 (Darling and Donoghue, 2014; Marr and Cathey, 2010), the industrial revolution and new means of transportation such as steamboats leading to the dispersal of rats in the year 1800 (Brygoo, 1966), as well as the intensification of agriculture especially poultry, pig and cattle farming in the year 1900 (Jones et al., 2013; Rogalski et al., 2017).

For COVID-19, the molecular divergence study between *SARS-CoV2* and other related bat SARS CoVs (*SARSr-CoV*; *RaTG13*) showed 4% genomic nucleotide variability. The novel functional site variations in the receptor binding domain (RBD) observed in *SARS-CoV2* and pangolin *SARS-CoVs* are likely caused by mutations and natural selection in addition to recombination.

4.4. Source of zoonotic diseases and species barrier

Currently, based on molecular analyses, bats are the main reservoir of different strains of *SARS-CoV* (2002) and *MERS-CoV* (2012), *SARS-CoV2* in 2019 (Wu et al., 2020b). These CoVs have crossed the species barrier and enzootically infect their intermediate hosts palm civet (*Paguma larvata*) and Dromedary or *Camelus dromedarius* respectively (Wit et al., 2016). While for *SARS-CoV* and *MERS-CoV* the intermediate hosts are known, questions still remain, whether *SARS-CoV2* would be transmitted directly from bats to humans or indirectly via an intermediate host (Wu et al., 2020b; Zhou et al., 2020). A second time, these CoVs will cross the species barrier by infecting humans and have become zoonotic (Wit et al., 2016). The explosion of these three CoV into pandemics in humans is due to the fact that they are mainly spread by human-to-human transmission in society or nosocomial (Liu et al., 2020).

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Authors Contributions

Designed and conceived: M.O.F; Wrote the manuscript: M.O.F and R.M.S

Competing Interests

The authors declare that no competing interest exists.

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