



A Review of Coronavirus Disease-2019 (COVID-19)

Qurrat ul ain Rana¹, Mohsin Khan², Abdul Haq¹, Syed saoud Zaidi³, Wasim Sajjad⁴,
Anwar Sheed Khan⁵, Sajid Ali⁶, Muhammad Tahir Khan⁷, Muhammad Irfan^{8*}

¹Department of Microbiology, Quaid-i-Azam University, Islamabad 45320, Pakistan

²School of Environment, Tsinghua University Beijing 100084 China

³Dow college of pharmacy Dow university of health Sciences Karachi, Pakistan

⁴State Key Laboratory of Cryosphere Science, Northwest Institute of Eco-Environment and Resources, Chinese Academy of Sciences, Lanzhou, China

⁵Department of Microbiology, Kohat University of Science and Technology Khyber Pakhtunkhwa, Pakistan

⁶Provincial TB Reference Laboratory, Peshawar, Pakistan

⁷Department of Bioinformatics and Biosciences, Capital University of Science and Technology, Islamabad Pakistan

⁸College of Dentistry, Department of Oral Biology, University of Florida, Gainesville, FL 32610

Key words: COVID-2019, Alphacoronavirus, Betacoronavirus, Gammacoronavirus, Deltacoronavirus, Prothrombin time.

<http://dx.doi.org/10.12692/ijb/16.5.265-279>

Article published on May 28, 2020

Abstract

In today's world new emerging infectious diseases, particularly those that directly infect respiratory system like Zika virus and severe acute respiratory syndrome (SARS) are posing a major threat to public health. Regardless of intensive research efforts being put, where, when and how these new diseases appear remains in the realm of unknown. A new disease called the coronavirus disease (COVID-19) which adversely affects the respiratory system has been reported recently in China particularly in Wuhan city of Hubei province. The ongoing worldwide outbreak of this disease was declared both pandemic and Public Health Emergency of International Concern by World Health Organization. The International Committee for the taxonomy of Viruses has named this virus as severe acute respiratory syndrome coronavirus 2 (SARSCoV-2). This virus initially originated in bats and then using, yet an unknown intermediary animal was acquired by humans in Wuhan, China in December 2019. There have been around 2,214,327 reported cases of coronavirus disease 2019 (COVID-2019) and 148,889 reported deaths to date (17/04/2020). The transmission of the disease is caused by encountering or inhalation of the infected droplets and the virus has an incubation time ranging from 2 to 14 days. The major symptoms of this disease include sore throat, cough, fever, fatigue, shortness of breath and malaise. Many people also remain asymptomatic. This review article highlights the details about coronavirus, its genome structure, disease, epidemiology, and its treatment.

* Corresponding Author: Muhammad Irfan ✉ irfanmuhammad@ufl.edu

Introduction

Coronaviruses are a group of viruses that are enveloped and have positive sense, single stranded and nonsegmented RNA genome (Wertheim *et al.*, 2013). Coronaviruses infect many vertebrates that are economically important including pigs and chicken however, there are six types of coronaviruses that are identified to cause respiratory diseases in human hosts as well. Out of these six coronaviruses that infect human, MERS-CoV Middle East respiratory syndrome and SARS-CoV severe acute respiratory syndrome coronavirus are both highly pathogenic zoonotic and are responsible for national and international outbreaks. The International Committee on Taxonomy of Viruses has classified coronaviruses under the order *Nidovirales*, family *Coronaviridae*, and subfamily *Coronavirinae*. *Coronavirinae* has been divided into four genera previously based on serology and now with genomic evidence. These four genera are *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*. The genus *Betacoronavirus* has been assigned four further distinct lineages (A-D). The six coronaviruses (HCoVs) that infect humans are distributed as *Alphacoronavirus* (HCoV-NL63 and HCoV-229E), while lineage A include (HCoV-HKU1, HCoV-OC43), lineage B (SARS-CoV), and MERS-CoV to lineage C *Betacoronavirus* (Fung and Liu, 2019) (Fig. 1).

Coronaviruses have a spherical shape which sometimes appear as pleomorphic and have a diameter of (80 to 120 nm). The electron microscope shows that the surface of the virion has club like projections which are made of trimeric spike (S) glycoprotein. Some *Betacoronaviruses* like HCoV-OC43 and HCoV-HKU1 also have shorter surface projection which are made up of dimeric hemagglutinin-esterase (HE) protein. Both surface proteins are transmembrane proteins that have a short endodomain and a large ectodomain. The envelope of the virus is sustained through glycoprotein (membrane M) which is actually the major structural protein which is embedded in the envelope by means of three transmembrane proteins (Fung *et al.*, 2020). In addition to membrane (M)

glycoprotein, small amount of transmembrane protein is also present in the envelope (Fung *et al.*, 2020). Lastly, the nucleoside (N) protein is attached to the genomic RNA of the virion in beads-on-a-string manner. The genome of coronavirus nonsegmented, positive sense and single stranded RNA that has an unusually large size which ranges from 27 to 32 kilobases. The genomic RNA of coronavirus is the usual 5'-capped and 3'-polyadenylated having multiple open reading frames (ORFs). The viral RNA is 3'-polyadenylated and 5'-capped and have numerous open reading frames (ORFs). The invariant gene order is 5'-replicase-S-E-M-N-3'-, with multiple small ORFs (encoding accessory proteins) distributed between the structural genes (Fig. 2). The replicase enzyme of coronavirus is determined by ORF1a and ORF1b (large overlapping ORFs) lodging around two-thirds of the viral genome and is directly converted from the genomic RNA. The important and structural viral genes are decoded from sgRNAs sub genomic RNAs produced throughout genome replication/transcription. Table 1 includes the factor associated to host responsible for coronavirus replication. This review article highlights the details about coronavirus, its genome structure, disease, epidemiology, and its treatment.

Discovery of HCoVs

In 1930 the first avian irresistible bronchitis virus i.eCoV was isolated. Distinctive CoVs were afterward isolated in infested rodents and native animals, together with cow, cats, mouse, turkey, dogs, and pig. CoVs were once accepted not a causative agent of human ailment, however this was reformed after the effective strain B814 of HCoV isolation from the examination of patients with basic cold from tracheal inoculum culture in 1962 (Kendall *et al.*, 1962). During the 1960s, a few novel HCoVs were depicted however no further portrayal was made in most cases (McIntosh *et al.*, 1967; Fung *et al.*, 2020). Both 229E and OC43 were considered as causal mediators of the common cold and URT disease, representing up to 30% of cases with basic cold (Fung *et al.*, 2020). 229E is a model strain segregated utilizing tracheal culture OC43 was segregated from organ culture and

consequent sequential passage in the brain of suckling mice. The clinical highlights of 229E and OC43 contamination were described in human volunteer investigation (Fung *et al.*, 2020). All around, customary sickness with HCoVs brings about slight common cold-like manifestations. Serious lower respiratory tract contamination grows just in immunocompromised patients (Pene *et al.*, 2003). Aside from a respiratory disease, 229E and OC43 were suspected to contaminate the central nervous system (CNS). This case was furthermore supported by the shortcoming of human neural primary culture to 229E and OC43 (Bonavia *et al.*, 1997). Notwithstanding, the impact of 229E and OC43 on the advancement and movement of various sclerosis anticipates further examinations.

In the pre-SARS time, it was commonly acknowledged that HCoVs just cause minor respiratory disease. This thought was changed after the rise of SARS-CoV. In November 2002, a viral respiratory ailment originally showed up in southern China and immediately spread to different nations, prompting more than 8,000 affirmed cases toward the end of the epidemic in June 2003, with a death pace of about 10 % (Perlman and Netland, 2009). The etiologic operator was recognized as SARS-CoV, a betacoronavirus (zoonotic) began in horseshoe bats that later adjusted to taint the transitional host palm civet and at last SARS patients create influenza like side effects and pneumonia, which in extreme cases lead to deadly respiratory failure and intense respiratory distress syndrome (Peiris *et al.*, 2003). Despite the fact that SARS-CoV contaminates various organs and causes systemic disease, indications certainly deteriorate as the virus is cleared, proposing that atypical immune response might trigger the pathogenesis of SARS-CoV (Perlman and Netland, 2009). A rich gene pool of bat SARS-related coronaviruses was found in a cave in Yunnan, China, featuring the need to get ready for future reappearance (Hu *et al.*, 2017).

MERS-CoV arose in Saudi Arabia in June 2012, as the causative agent of a SARS-like respiratory ailment (de

Groot *et al.*, 2013). Albeit human-to-human transmission is viewed as constrained, MERS-CoV has caused two significant flare-ups in Saudi Arabia (2012) and South Korea (2015), with the worldwide affirmed cases surpassing 2,000 and a death pace of 35% (Chafekar and Fielding, 2018). Old individuals tainted with MERS-CoV, especially those with comorbidities, for the most part grow increasingly serious and some of the time deadly ailment (Graham *et al.*, 2013). Like SARS-CoV, MERS-CoV began in bats, yet it later adjusted to dromedary camels as transitional hosts (Corman *et al.*, 2014).

In late December 2019, another viral disease stood out in Wuhan, the capital of Hubei, China. Afterward, it was uncovered that the virus answerable for causing the contaminations was infectious between human. By early January, terms like "the new coronavirus" and "Wuhan coronavirus" were in like manner use. On February 11, 2020, an ordered assignment "extreme intense respiratory disorder coronavirus (SARS-CoV-2) turned into the official way to allude to the infection strain, that was recently named as 2019-nCoV and Wuhan coronavirus. Inside a couple of hours around the same day, the WHO authoritatively renamed the infection as COVID-19 (Baig *et al.*, 2020).

The 2019 novel CoV (SARS-CoV-2) is the freshest expansion to human CoVs (HCoVs) that likewise incorporate 229E, OC43, HKU1, NL63, severe acute respiratory syndrome (SARS) CoV, and Middle East respiratory syndrome (MERS) CoV. While 229E and NL63 have a place with Alphacoronavirus, others are individuals in the class of Betacoronavirus (Fung *et al.*, 2020). New cases are identified, primarily in other Asian countries and in many countries such as the Europe, Africa, trans-oceanic USA (Table 2). Presently, no immunization or explicit antiviral medication has been affirmed for either SARS-CoV, MERS-CoV or COVID-19.

Virology-Pathogenesis

Coronaviruses are infectious agents whose genome structure is most popular among all RNA viruses.

About two-thirds of RNA have encodes viral polymerase (RdRp), the RNA production ingredients, also, two enormous nonstructural polypeptides that are not associated with in host response modulation (ORF1a-ORF1b). The other one-third of the genome encodes four basic proteins envelope (E), (spike (S), membrane (M) ve nucleocapsid (N) along with

additional aid proteins (Luk *et al.*, 2019; Sahin *et al.*, 2020). Despite the fact that the length of the CoV genome shows high inconstancy for ORF1a/ORF1b and four basic proteins, it is for the most part connected with the number and size of adornment proteins (Sahin *et al.*, 2020).

Table 1. Host factors involved in HCoV replication. (Fung and Liu 2019).

Replication stage	Host factor (s)	HCoV (other CoV)	Function
Attachment and entry	APN	HCoV-229E	Cellular receptor
	ACE2	SARS-CoV, HCoV-NL63	Cellular receptor
	DPP4	MERS-CoV	Cellular receptor
	9-O-acetylated sialic acid	HCoV-OC43, HCoV-HKU1	Cellular receptor
	Cathepsin L	SARS-CoV	Cleave and activate S protein
	Furin	MERS-CoV, (IBV)	Cleave and activate S protein
	VCP	HCoV-229E, (IBV)	Facilitate virus release from early endosomes during entry
	IFITM	SARS-CoV, MERS-CoV, HCoV-229E, HCoV-NL63	Restrict virus entry
	IFITM2/IFITM3	HCoV-OC43	Facilitate virus entry
Translation of replicase and RTC assembly	Annexin A2	(IBV)	Bind to RNA pseudoknot and regulate ribosomal frameshifting
	GBF1 and ARF1	(MHV)	Facilitate the formation of double-membrane vesicle
Genome replication and transcription	GSK3	SARS-CoV, (MHV-JHM)	Phosphorylate N protein and facilitate viral replication
	DDX1	(MHV-JHM)	Facilitate template switching and synthesis of genomic RNA and long sgRNAs
	hnRNPA1	SARS-CoV	Regulate viral RNA synthesis
	ZCRB1	(IBV)	Bind to 5' UTR of the viral genome
	Mitochondrial aconitase	(MHV)	Bind to 3' UTR of the viral genome
	PABP	(Bovine CoV)	Bind to poly(A) tail of the viral genome
Translation of structural proteins	N-linked glycosylation enzymes	SARS-CoV	Modify S and M protein; N-linked glycosylation of the S protein facilitates lectin-mediated virion attachment and constitutes some neutralizing epitopes
	O-linked glycosylation enzymes	(MHV)	Modify M protein; O-linked glycosylation of the M protein affects interferon induction and virus replication in vivo
	ER chaperones	SARS-CoV	Proper folding and maturation of S protein
Virion assembly and release	Tubulin	HCoV-229E, HCoV-NL63, (TGEV)	Bind to cytosolic domain of S protein; facilitate particle assembly and release
	β -Actin	(IBV)	Bind to M protein; facilitate particle assembly and release
	Vimentin	(TGEV)	Bind to N protein; facilitate particle assembly and release
	Filamin A	(TGEV)	Bind to S protein; facilitate particle assembly and release

RTC= Replication Transcription Complex; sgRNA= subgenomic RNA.

The initial phase in infection contamination is the collaboration of sensitive human cells with Spike Protein. Genome encoding happens in the wake of entering to the cell and encourages the outflow of the

genes, that encode helpful extra proteins, which advance the adjustment of CoVs to their human host (Sahin *et al.*, 2020). Genome changes ensuing from gene insertion, recombination, gene exchange or

deletion are common among CoVs, and this will happen in future episodes as in past epidemics. Because of the examinations, the CoV subfamily is quickly extending with new age sequencing applications that improve the identification and meaning of novel CoV species. All in all, CoV arrangement is persistently evolving. As indicated by the latest grouping of The International Committee

on Taxonomy of Viruses (ICTV), there are four genera of thirty-eight exceptional species. SARS-CoV and MERS-CoV that connect to the host cell individually tie to cell receptor angiotensin-converting enzyme 2 (SARS-CoV associated) and cellular receptor of dipeptidylm peptidase 4 (MERS-CoV associated) (Lambeir *et al.*, 2003).

Table 2. The number of cases and death of COVID-19 outbreak according to World Health Organization (WHO) situation (06/04/2020).

SL. No.	Country	Cases	Death	Region
1	USA	680,541	34,723	North America
2	Spain	184,948	19,315	Europe
3	Italy	168,941	22,170	Europe
4	France	165,027	17,920	Europe
5	Germany	138,369	4,105	Europe
6	U. K	108,692	14,576	Asia
7	China	82,692	4,632	Asia
8	Iran	79,494	4,958	Europe
9	Turkey	78,546	1,769	Asia/Europe
10	Belgium	36,138	5,163	Europe

In the wake of entering the cell, the viral RNA establishes itself in the cytoplasm. Genomic RNA is polyadenylated and encapsulated and encodes numerous basic and non-basic polypeptide genes. These polyproteins are part by proteases that display chymotrypsin-like activity (Lambeir *et al.*, 2003).

The subsequent complex initiates (-) RNA assembly through both replication and transcription. At the time of replication, full-length (-) RNA copies of the genome are fashioned and utilized as a format for full-length (+) RNA genomes (Sahin *et al.*, 2020). At the time of transcription, a subset of 7-9 sub-genomic RNAs, including those encoding every single basic protein, are delivered by intermittent transcription. Through genomic RNA and R protein the viral nucleocapsids are combined in the cytoplasm and then are budded into the lumen of the endoplasmic reticulum. Exocytosis releases the virions and its contaminate intestines, kidney cells, T lymphocytes and liver cells, and LRT(lower respiratory tract) , where they structure the fundamental indications and

signs (Lambeir *et al.*, 2003). Macrophage and dendritic cell can be influenced by MERS-CoV. T lymphocytes are likewise an objective for the pathogen because of the characteristic CD26 rosettes.

This virus can make the antiviral T-cell reaction sporadic because of the incitement of T-cell apoptosis, consequently causing a breakdown of the invulnerable framework (Chu *et al.*, 2014; Zhou *et al.*, 2014).

Patients contaminated with COVID-19 demonstrated higher leukocyte numbers, anomalous respiratory discoveries, and expanded degrees of plasma pro inflammatory cytokines. One of the COVID-19 case reports demonstrated a patient at 5 days fever presented with a cough, coarse breathing sounds of the two lungs, and a body temperature of 39.0 °C.

The patient's sputum demonstrated real-time polymerase chain reaction results that affirmed COVID-19 disease (Lei *et al.*, 2020).

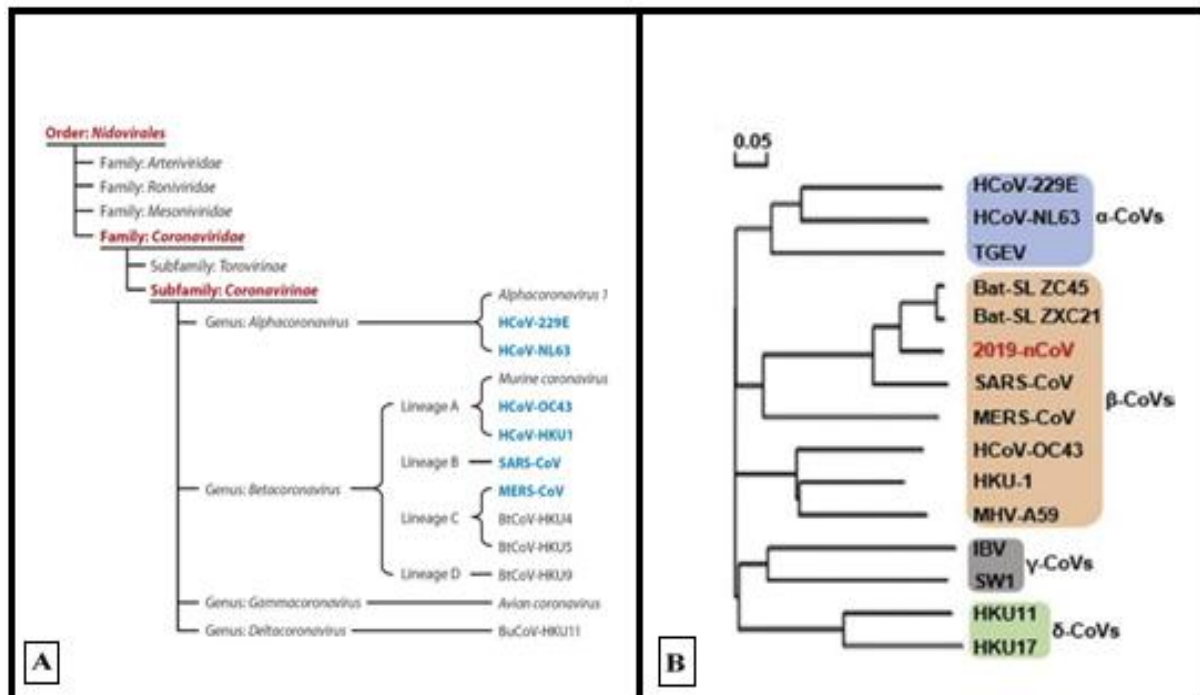


Fig. 1. A. Taxonomy of HCoVs: A) Classification system (coronaviruse and HCoV). (Fung and Liu 2019) Known HCoVs (6) are represented in blue.

The research center investigations demonstrated leucopenia with leukocyte checks of 2.91×10^9 cells/L of which 70.0% were neutrophils. Also, an estimation of 16.16 mg/L of blood C-receptive protein was noted which is over the ordinary range (0–10 mg/L). Elevated ESR and D-dimer were likewise detected (Lei *et al.*, 2020).

The principle pathogenesis of COVID-19 contamination as a respiratory framework focusing on infection was extreme pneumonia, RNAemia, joined with the rate of ground-glass opacities, and intense cardiac injury (Huang *et al.*, 2020).

Altogether high blood levels of cytokines and chemokines were noted in patients with COVID-19 contamination that comprised IL1RA, IL7, IL8, IL1-β, IL9, IL10, basic GCSF, GMCSF, FGF2, IFNγ, IP10, PDGFB, TNFα, VEGFA MCP1, MIP1α and MIP1β. A portion of the intense cases that were confessed to the emergency unit high levels of pro-inflammatory cytokines together with IP10, GCSF, MCP1, MIP1α, IL2, IL7, IL10 and TNFα are contemplated to advance illness seriousness (Huang *et al.*, 2020; Rothan and Byraredy, 2020).

Epidemiology

Geographic distribution

All around, more than a million affirmed instances of COVID-19 have been accounted for. Refreshed case includes in English can be found on the World Health Organization and European Centre for Disease Prevention and Control websites. A shrewd map featuring affirmed cases throughout the world can be found (<https://coronavirus.jhu.edu/map.html>).

Since the main reports of cases from Wuhan, a city in the Hubei Province of China, toward the finish of 2019, more than 80,000 COVID-19 cases have been accounted for in China, with most of those from Hubei and encompassing regions.

A joint World Health Organization (WHO)-China fact discovering crucial that the scourge in China topped between late January and early February 2020 and the pace of new cases diminished considerably by early March (WHO 16 March 2020).

Though, cases have been accounted for in all countries, aside from Antarctica, and have been consistently ascending far and wide.

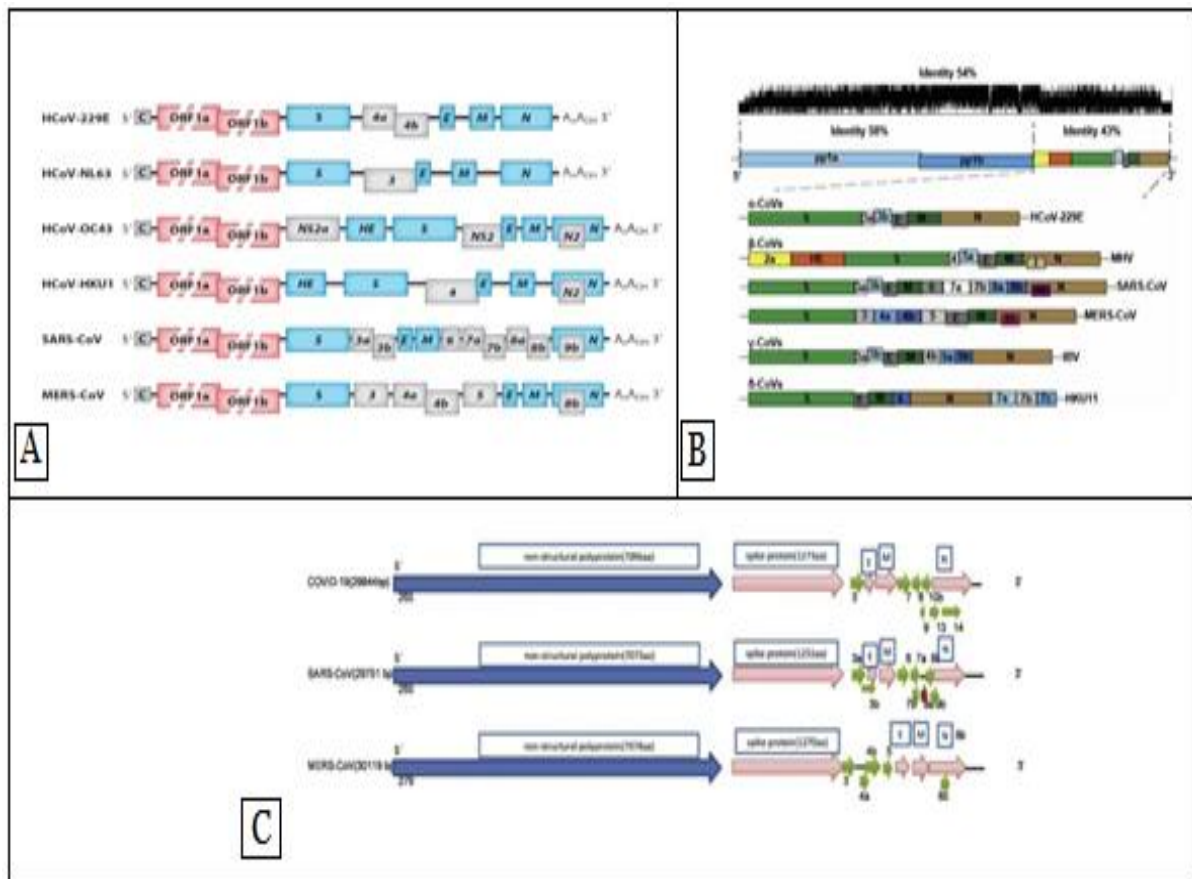


Fig. 2. Genome structure of human coronaviruses (HCoVs).

A) Schematic diagram showing the genome structure of six known HCoVs (not to scale). The 5'-cap structure (5'-C) and 3'-polyadenylation (AnAOH-3') are indicated. The open reading frame 1a (ORF1a) and ORF1b are represented as shortened red boxes. The genes encoding spike (S), envelope (E), membrane (M), nucleocapsid (N), and hemagglutinin-esterase (HE) are shown as blue boxes. The genes encoding accessory proteins are shown as gray boxes. (Fung and Liu 2019).

B) The genome structure of four genera of coronaviruses:

C) The 5' UTR and 3' UTR and coding region of COVID-19, SARS-CoV, and MERS-CoV (Mousavizadeh and Ghasemi. 2020).

Route of transmission

Comprehension of the transmission hazard is deficient. Epidemiologic examination in Wuhan toward the start of the outbreak recognized an underlying relationship with a seafood market that sold live animals, where most patients had worked or visited, and which was in this way shut for cleansing. Nevertheless, as the flare-up advanced, individual to-individual spread turned into the fundamental method of transmission (Fig. 3) while Fig 4 shows timeline of 2019-nCoV virus. Individual to-individual spread of extreme intense respiratory disorder coronavirus 2 (SARS-CoV-2) is thought to happen fundamentally by means of respiratory droplets,

resembling the spread of influenza. With globule transmission, virus released in the respiratory discharges when an individual with contamination talks, coughs or sneezes can taint someone else in the event that it reaches the mucous layers; disease can likewise happen on the off chance that an individual contacts a contaminated surface and, at that point contacts their eyes, nose, or mouth. Droplets ordinarily don't travel in excess of six feet (around two meters) and don't hold up in the air. Though one letter to the article administrator delineated an assessment in which SARS-CoV-2 remained reasonable in experimentally created aerosols for at any rate three hours, the hugeness of this to the

investigation of illness transmission of COVID-19 and its clinical implications are ill defined (van Doremalen *et al.*, 2020). Given the current weakness as for transmission frameworks, airborne shields are recommended in explicit conditions. SARS-CoV-2 RNA has been perceived in blood and stool models

(Chen *et al.*, 2020; Tang *et al.*, 2020). Live virus has been refined from stool at times (Wang *et al.*, 2020b), yet as per a joint WHO-China report, fecal-oral transmission didn't seem, by all accounts, to be a noteworthy factor in the spread of disease (McIntosh *et al.*, 2020).

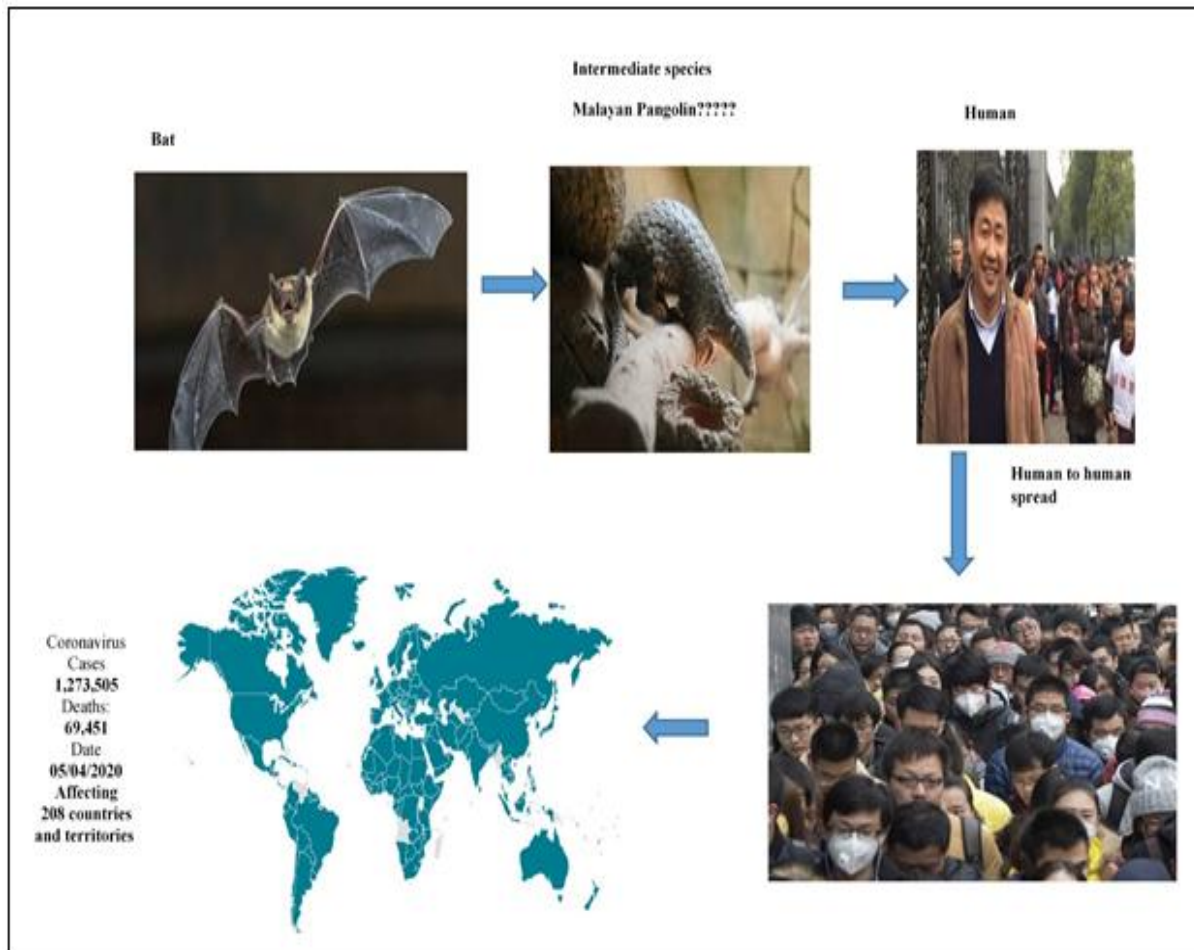


Fig. 3. Sars-Cov-2 interspecies transmission, the virus originated in bats. The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d.

Period of infectivity

The interim during which a person with COVID-19 is irresistible is dubious. Most information advising this issue are from examines assessing viral RNA discovery from respiratory and different specimens. Though, detection of viral RNA does not really demonstrate the nearness of irresistible virus. Viral RNA levels from upper respiratory examples seem, by all accounts, to be higher not long after symptom onset contrasted and later in the illness (To *et al.*, 2020; Wölfel *et al.*, 2020; Zou *et al.*, 2020). Moreover, in an investigation of nine patients with

gentle COVID-19, irresistible infection was detached from naso/oropharyngeal and sputum examples during the principal first week of illness, however not after this interim, in spite of proceeded with high popular RNA levels at these locales (Wölfel *et al.*, 2020). These discoveries raise the likelihood that transmission may be more probable in the prior phase of disease, yet extra information is expected to affirm this speculation.

The span of viral shedding is additionally factor; there gives off an impression of being a wide range, which

may rely upon seriousness of sickness. In one investigation of 21 patients with mild illness (no hypoxia), 90 percent had rehashed negative viral RNA tests on nasopharyngeal swabs by 10 days after the beginning of symptoms; tests were positive for longer in patients with progressively extreme sickness (Liu *et al.*, 2020). In another investigation of 137 patients who endure COVID-19, the middle length of viral RNA shedding from oropharyngeal examples was 20 days (scope of 8 to 37 days) (Zhou *et al.*,

2020). As referenced above, discernible viral RNA doesn't constantly associate with separation of irresistible virus, and there might be a limit of viral RNA level underneath which infectivity is impossible.

In the investigation of nine patients with gentle COVID-19 depicted above, irresistible infection was not identified from respiratory examples when the viral RNA level was $<10^6$ copies/mL (Wölfel *et al.*, 2020).

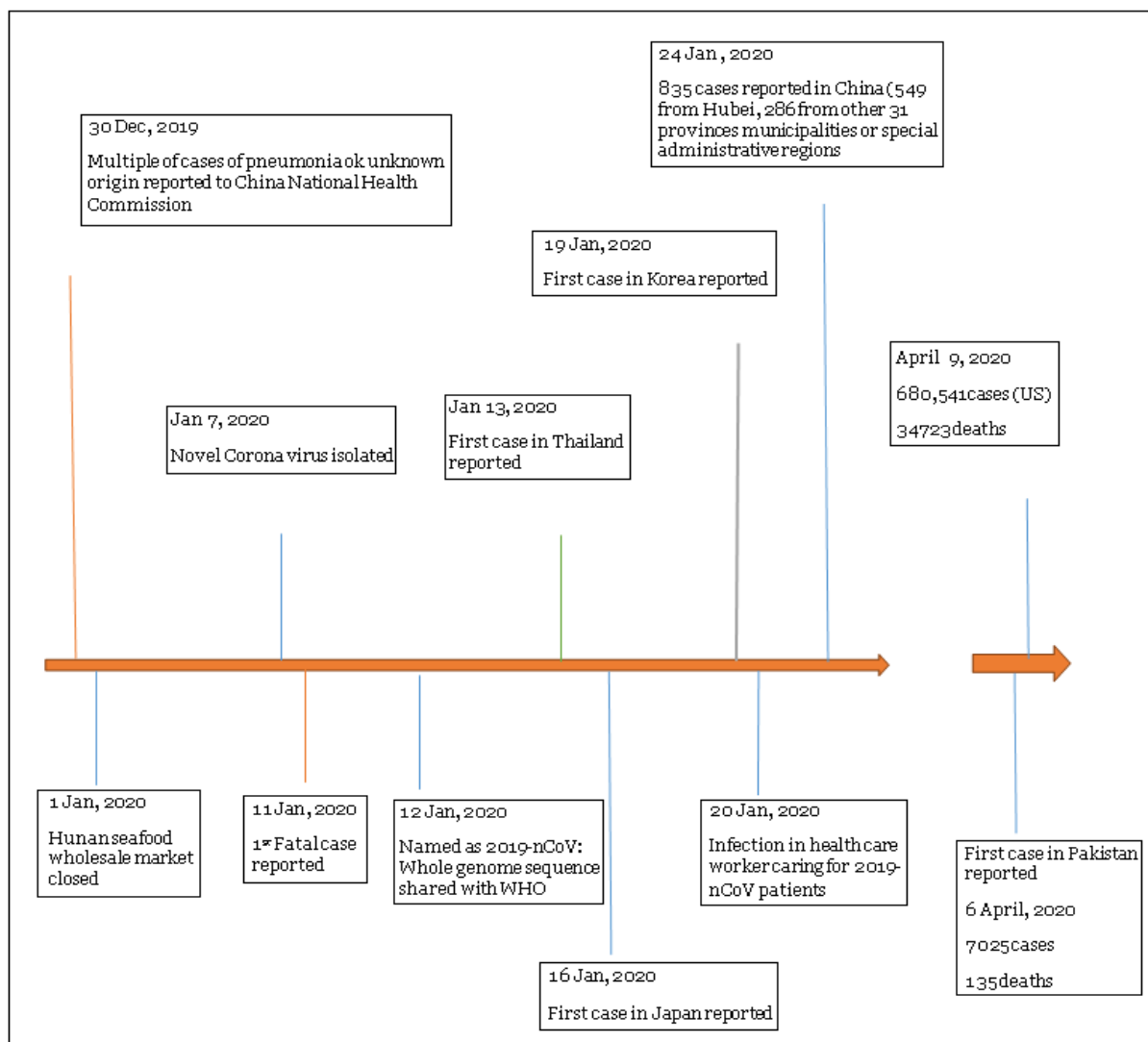


Fig. 4. Timeline of 2019-nCoV.

The revealed paces of transmission from a person with symptomatic contamination change by area and disease control intercessions. As per a joint WHO-China report, the pace of optional COVID-19 ranged from 1 to 5 percent among a huge number of close contacts of affirmed patients in China (McIntosh *et*

al., 2020). Among group individuals on a voyage transport, 2 percent created affirmed contamination (Kakimoto *et al.*, 2020a). In the United States, the symptomatic optional assault rate was 0.45 percent among 445 close contacts of 10 affirmed patients (Kakimoto *et al.*, 2020b).

Transmission of SARS-CoV-2 from asymptomatic people (or people in incubation period) has likewise been depicted (Bai *et al.*, 2020; Burke *et al.*, 2020; Hu *et al.*, 2020; Rothe *et al.*, 2020; Yu *et al.*, 2020). In any case, the degree to which this happens stays obscure. In an investigation of 157 privately gained COVID-19 cases in Singapore, transmission during the incubation period was assessed to represent 6.4 percent; in such cases, the exposures happened one to three days before side effect advancement (Qian *et al.*, 2020). Enormous scope serologic screening might have the option to give a superior feeling of the extent of asymptomatic diseases and advise epidemiologic examination; a few serologic tests for SARS-CoV-2 are being worked on, and one has been affirmed by the US Food and Drug Administration Food and Drug Administration (FDA) (Li *et al.*, 2020b).

Diagnosis

Suspect case is characterized as one with sore throat, fever and cough who has history of movement to China or different territories of constant neighborhood transmission or any contact with peoples having any comparable travel history or those with affirmed COVID-19 contamination. Though, cases might be asymptomatic or even without fever. An affirmed case is a speculate case with a positive molecular test.

Explicit analysis is by explicit molecular tests of samples (endotracheal aspirates/ nasopharyngeal swab// sputum/ throat swab and bronchoalveolar lavage). Virus may likewise be recognized in the stool and blood (serious cases). It must be recollected that the multiplex PCR boards as of now accessible do exclude the COVID-19.

Other lab examinations are normally vague. The white cell check is generally ordinary or low. There might be lymphopenia in extreme disease. procalcitonin levels are generally ordinary while platelet count is typically ordinary or somewhat low. A high procalcitonin level may show a bacterial co-disease. The CRP and ESR are commonly raised. The creatinine, ALT/AST, CPK, prothrombin time, D-

dimer, and LDH might be raised and elevated levels are related with serious disease (Singhal, 2020).

The chest X-ray (CXR) ordinarily shows bilateral penetrates however might be typical in early malady. The CT is increasingly delicate and explicit. CT imaging for the most part shows invades, sub segmental consolidation and ground glass opacities. It is additionally strange in asymptomatic patients/patients with no clinical proof of lower respiratory tract contribution. Indeed, irregular CT scans have been utilized to analyze COVID-19 in speculate cases with negative molecular diagnosis; a considerable lot of these patients had positive sub-atomic tests on rehash testing (Singhal, 2020).

Differential Diagnosis

The differential determination incorporates a wide range of respiratory viral contaminations [respiratory syncytial virus (RSV), influenza, parainfluenza, adenovirus, non COVID-19 coronavirus, human metapneumovirus], atypical life forms (chlamydia, mycoplasma) and bacterial diseases. It is beyond the realm of imagination to expect to separate COVID-19 from these diseases clinically or through routine lab tests. Consequently, travel history gets significant. Be that as it may, as the epidemic spreads, the movement history will get unessential.

Treatment

Treatment is basically steady and symptomatic. The initial step is to guarantee satisfactory seclusion (examined later) to forestall transmission to different contacts, patients, and social insurance laborers. Home administration is fitting for patients with non-serious contamination (e.g; cough, fever and/or myalgias without dyspnea) who can be sufficiently disconnected in the outpatient setting (McIntosh *et al.*, 2020). The board of such patients should concentrate on counteraction of transmission to other people and checking for clinical weakening, which should provoke hospitalization.

Outpatient administration is primarily supportive with antipyretics, hydration, and analgesics, if

essential. Outpatients with COVID-19 should remain at home and attempt to isolate themselves from others and animals in the household. They should wear a face spread when in a similar room (or vehicle) as others and when introducing to medicinal services settings. Sterilization of every now and again contacted surfaces is additionally significant.

A few patients with suspected or archived COVID-19 have extreme disease that warrants hospital care. Management of such patients comprises of guaranteeing fitting contamination control. Patients with serious illness regularly need oxygenation support. High-stream oxygen and noninvasive positive weight ventilation have been utilized, yet the security of these measures is questionable, and they ought to be viewed as airborne producing strategies that warrant explicit detachment safety measures.

The WHO and CDC suggest glucocorticoids not be utilized in patients with COVID-19 pneumonia except if there are different signs (e.g; worsening of incessant obstructive aspiratory infection). Glucocorticoids have been related with an expanded hazard for mortality in patients with flu and postponed viral freedom in patients with Middle East respiratory disorder coronavirus (MERS-CoV) disease. In spite of the fact that they were generally utilized in the executives of severe acute respiratory syndrome (SARS), there was nothing more than a bad memory proof for advantage, and there was convincing proof of unfriendly short-and long term harm (Russell *et al.*, 2020).

A few clinicians have recommended the utilization of non-steroidal anti-inflammatory drugs (NSAIDs) primarily throughout sickness may negatively affect ailment result (Day, 2020). These apprehensions are grounded on unreliable reports of a few young patients who received NSAIDs right off the bat over the span of contamination and experienced serious ailment. In any case, there have been no clinical or populace-based information that legitimately address the danger of NSAIDs. The European Medicines Agency (EMA) and the WHO don't suggest that

NSAIDs be maintained a strategic distance from when clinically demonstrated (McIntosh *et al.*, 2020). Given the vulnerability, we recommend acetaminophen as the favored antipyretic agent, if conceivable, and if NSAIDs are required, the most reduced successful portion ought to be utilized. In any case, we do not recommend that NSAIDs be halted in patients who are on them constantly for different conditions, except if there are different motivations to stop them (e.g; renal injury, gastrointestinal bleeding).

A few randomized preliminaries are in progress to assess the adequacy of remdesivir for moderate or extreme COVID-19 (McIntosh *et al.* 2020). Remdesivir is a novel nucleotide analogue that has activity against coronaviruses infections (including SARS and MERS-CoV)(Sheahan *et al.* 2017; Wang *et al.* 2020a).

Both chloroquine and hydroxychloroquine have been accounted for to hinder SARS-CoV-2 in vitro, in spite of the fact that hydroxychloroquine seems to have progressively intense antiviral activity (Lescure *et al.* 2020).

Clinical information assessing hydroxychloroquine or chloroquine is constrained, and their adequacy against SARS-CoV-2 is obscure.

Prevention

Since as of now there are no affirmed medications for this contamination, counteraction is critical. A few properties of this infection make anticipation troublesome specifically, non-specific structures of the disease, the infectivity even before beginning of indications in the incubation period, tropism for mucosal surfaces such as the conjunctiva, transmission asymptomatic individuals, extended period of the illness, extensive incubation period, and transmission much after clinical recuperation.

In general, transport and development of the patient outside of their room ought to be constrained to restoratively fundamental purposes. The ventilation

at home ought to be acceptable with daylight to take into consideration pulverization of virus. Patients ought to be approached to use surgical mask and exercise cough hygiene. Caregivers should wear a surgical mask when in a similar room as patient and use hand cleanliness each 15–20 min.

The most serious hazard in COVID-19 is transmission to human services laborers (Chang *et al.*, 2020). The doctors who originally cautioned about the infection have passed on as well. It is imperative to secure human services laborers to guarantee progression of care and to forestall transmission of disease to different patients. While COVID-19 transmits as a droplet pathogen and is set in Category B of irresistible agents (profoundly pathogenic SARS and H5N1), by the China National Health Commission, disease control measures prescribed are those for class A agents (plague, cholera). Patients ought to be set in independent rooms or cohorted together.

The rooms and surfaces and hardware ought to experience ordinary cleaning ideally with sodium hypochlorite. Social insurance laborers ought to be given fit tested N95 masks and defensive costumes and goggles. Airborne transmission insurances ought to be taken during vaporized processes such as suction, intubation, and tracheostomies. All contacts including social insurance laborers ought to be observed for improvement of side effects of COVID-19. Patients can be released from separation once they are afebrile for minimum 3 d and have two back to back negative molecular tests at 1 d sampling interim (Li *et al.*, 2020a).

At the network level, individuals ought to be approached to keep away from swarmed zones and delay trivial travel to places with continuous transmission. They ought to be approached to rehearse coughing in tissue/sleeve instead of hands and exercise hand cleanliness much of the time each 15–20 min. Patients with respiratory side effects ought to be approached to utilize surgical masks. The utilization of mask by physically well individuals in community places has not appeared to ensure against

respiratory viral contaminations and is as of now not prescribed by WHO. Nonetheless, in China, general society has been approached to wear masks in community and especially in congested spaces and enormous scope get-togethers are precluded (amusement parks and so forth). China is likewise considering acquainting enactment with prohibiting selling and exchanging of wild animals (Li *et al.*, 2020a; Singhal, 2020).

The global reaction has been emotional. At first, there were enormous travel limitations to China and individuals coming back from China/ emigrant from China are being assessed for clinical indications, segregated, and tried for COVID-19 for 2 wks.

Regardless of whether asymptomatic. Notwithstanding, presently with quick overall spread of the infection these movement limitations have stretched out to different nations. Regardless of whether these endeavors will prompt easing back of viral spread isn't known. An applicant vaccine is a work in progress.

Conclusion

This new virus episode has tested the financial, clinical and general wellbeing foundation of China and somewhat, of different nations particularly, its neighbors. Time alone will tell how the infection will affect lives here in the world. More so, future episodes of viruses and pathogens of the zoonotic beginning stage are presumably going to continue. Consequently, aside from controlling this episode, endeavors ought to be made to devise complete measures to forestall future flare-ups of zoonotic beginning.

Acknowledgments

The authors would like to thank the *Quaid-I-Azam University Islamabad Pakistan*.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare no potential conflicts of interest to disclose.

References

Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, Wang M. 2020. Presumed Asymptomatic Carrier Transmission of COVID-19. *Journal of American Medical Association* **323**, 1339-1343.
<http://dx.doi.org/10.1001/jama.2020.2565>.

Baig AM, Khaleeq A, Ali U, Syeda H. 2020. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host–Virus Interaction, and Proposed Neurotropic Mechanisms. *ACS chemical neuroscience* **11**(7), 995-998.
<http://dx.doi.org/10.1021/acscchemneuro.0c00122>.

Bonavia A, Arbour N, Yong VW, Talbot PJ. 1997. Infection of primary cultures of human neural cells by human coronaviruses 229E and OC43. *Journal of virology* **71**, 800-806.

Burke RM. 2020. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. *MMWR Morb Mortal Wkly Rep* **69**, 245-246
<http://dx.doi.org/10.15585/mmwr.mm6909e1>.

Chafekar A, Fielding BC. 2018. MERS-CoV: understanding the latest human coronavirus threat. *Viruses* **10**(2), pii: E93.
<http://dx.doi.org/10.3390/v10020093>.

Chang Xu H, Rebaza A, Sharma L, Dela Cruz CS. 2020. Protecting health-care workers from subclinical coronavirus infection. *Lancet Respiratory Medicine* **8**, e13
[http://dx.doi.org/10.1016/s2213-2600\(20\)30066-7](http://dx.doi.org/10.1016/s2213-2600(20)30066-7).

Chen W. 2020. Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity. *Emerging Microbes & Infections* **9**, 469-473.

Chu H. 2014. Productive replication of Middle East respiratory syndrome coronavirus in monocyte-derived dendritic cells modulates innate immune response. *Virology* **454**, 197-205.

Corman VM. 2014. Rooting the phylogenetic tree of middle East respiratory syndrome coronavirus by characterization of a conspecific virus from an African bat. *Journal of virology* **88**, 11297-11303.

Day M. 2020. Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists. *British Medical Journal* 368:m1086.
<http://dx.doi.org/10.1136/bmj.m1086>

de Groot RJ. 2013. Commentary: Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. *Journal of virology* **87**, 7790-7792.

Fung SY, Yuen KS, Ye ZW, Chan CP, Jin DY. 2020. A tug-of-war between severe acute respiratory syndrome coronavirus 2 and host antiviral defence: lessons from other pathogenic viruses. *Emerging microbes & infections* **9**, 558-570.

Fung TS, Liu DX. 2019. Human Coronavirus: Host-Pathogen Interaction. *Annual review of microbiology* **73**, 529-557.

Graham RL, Donaldson EF, Baric RS. 2013. A decade after SARS: strategies for controlling emerging coronaviruses. *Nature Reviews Microbiology* **11**, 836-848.

Hu B. 2017. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS pathogens*.
<https://doi.org/10.1371/journal.ppat.1006698N>.

Hu Z. 2020. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China *Science China Life Sciences*.
<http://dx.doi.org/10.1007/s11427-020-1661-4>

Huang C. 2020 Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* **395**, 497-506.

Kakimoto K, Kamiya H, Yamagishi T, Matsui T, Suzuki M, Wakita T. 2020a. Initial investigation of transmission of COVID-19 among crew members during quarantine of a cruise ship—Yokohama,

Japan, February 2020. Centers for Disease Control and Prevention **69**(11), 312-313.

Kakimoto K, Kamiya H, Yamagishi T, Matsui T, Suzuki M, Wakita T. 2020b. Initial Investigation of Transmission of COVID-19 Among Crew Members During Quarantine of a Cruise Ship - Yokohama, Japan, February 2020. MMWR Morb Mortal Wkly Rep **69**, 312-313
<http://dx.doi.org/10.15585/mmwr.mm6911e2>

Kendall E, Bynoe M, Tyrrell D. 1962. Virus isolations from common colds occurring in a residential school. British medical journal **2**(5297), 82-86.
<http://dx.doi.org/10.1136/bmj.2.5297.82>.

Lambeir AM, Durinx C, Scharpé S, De Meester I. 2003. Dipeptidyl-peptidase IV from bench to bedside: an update on structural properties, functions, and clinical aspects of the enzyme DPP IV. Critical reviews in clinical laboratory sciences **40**, 209-294.

Lei J, Li J, Li X, Qi X. 2020. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology **295**(1), 18.
<http://dx.doi.org/10.1148/radiol.202000236>.

Lescure FX. 2020. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. Lancet Infectious Disease
[http://dx.doi.org/10.1016/s1473-3099\(20\)30200-0](http://dx.doi.org/10.1016/s1473-3099(20)30200-0).

Li J. 2020a. Game consumption and the 2019 novel coronavirus. Lancet Infectious Disease **20**(3), 275-276.
[http://dx.doi.org/10.1016/s1473-3099\(20\)30063-3](http://dx.doi.org/10.1016/s1473-3099(20)30063-3)

Li Z. 2020b. Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. Journal of Medical Virology 1-7.
<http://dx.doi.org/10.1002/jmv.25727>

Liu Y. 2020. Viral dynamics in mild and severe cases of COVID-19. The Lancet Infectious Diseases.
[https://doi.org/10.1016/S1473-3099\(20\)302322](https://doi.org/10.1016/S1473-3099(20)302322).

Luk HK, Li X, Fung J, Lau SK, Woo PC. 2019. Molecular epidemiology, evolution and phylogeny of SARS coronavirus. Infection, Genetics and Evolution **71**, 21-30.
<http://dx.doi.org/10.1016/j.meegid.2019.03.001>.

McIntosh K, Dees JH, Becker WB, Kapikian AZ, Chanock RM. 1967. Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. Proceedings of the National Academy of Sciences of the United States of America **57**(4), 933-940.
<http://dx.doi.org/10.1073/pnas.57.4.933>.

McIntosh K, Hirsch MS, Bloom A. 2020. Coronavirus disease 2019 (COVID-19). UpToDate. Hirsch MS, Bloom A (Eds.). Accessed Mar 5.

Peiris J. 2003. Coronavirus as a possible cause of severe acute respiratory syndrome. The Lancet **361**, 1319-1325.

Pene F. 2003. Coronavirus 229E-related pneumonia in immunocompromised patients. Clinical infectious diseases **37**, 929-932.

Perlman S, Netland J. 2009. Coronaviruses post-SARS: update on replication and pathogenesis. Nature reviews microbiology **7**, 439-450.

Qian G. 2020. A COVID-19 Transmission within a family cluster by presymptomatic infectors in China. Clinical Infectious Disease
<http://dx.doi.org/10.1093/cid/ciaa316>.

Rothan HA, Byrareddy SN. 2020. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of Autoimmunity **109**, 102433.

Rothe C. 2020. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. N England Journal of Medicine **382**, 970-971
<http://dx.doi.org/10.1056/NEJMc2001468>.

Russell CD, Millar JE, Baillie JK. 2020. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet **395**, 473-475.
[http://dx.doi.org/10.1016/s0140-6736\(20\)30317-2](http://dx.doi.org/10.1016/s0140-6736(20)30317-2).

- Sahin AR.** 2020. 2019 Novel Coronavirus (COVID-19) Outbreak: A Review of the Current Literature. *Eurasian Journal of Medicine and Oncology* **4**, 1-7.
- Sheahan TP.** 2017. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. *Science translational medicine* **28(9)**, 396. pii: eaal3653.
<http://dx.doi.org/10.1126/scitranslmed.aal3653>.
- Singhal T.** 2020. A Review of Coronavirus Disease-2019 (COVID-19). *Indian Journal of Pediatric* **87**, 281-286
<http://dx.doi.org/10.1007/s12098-020-03263-6>.
- Tang A.** 2020. Detection of Novel Coronavirus by RT-PCR in Stool Specimen from Asymptomatic Child, China. *Emerging infectious diseases* **26**.
- To KKW.** 2020. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *The Lancet Infectious Diseases* **20(5)**, 565-574.
[http://dx.doi.org/10.1016/S1473-3099\(20\)30196-1](http://dx.doi.org/10.1016/S1473-3099(20)30196-1).
- Van Doremalen N.** 2020. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *New England Journal of Medicine* **382**, 1564-1567.
<http://dx.doi.org/10.1056/NEJMc2004973>.
- Wang M.** 2020a. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Research* **30**, 269-271.
<http://dx.doi.org/10.1038/s41422-020-0282-0>
- Wang W.** 2020b. Detection of SARS-CoV-2 in different types of clinical specimens. *Journal of American Medical Association*.
<http://dx.doi.org/10.1001/jama.2020.3786>.
- Wertheim JO, Chu DK, Peiris JS, Pond SLK, Poon LL.** 2013. A case for the ancient origin of coronaviruses. *Journal of Virology* **87**, 7039-7045.
- Wölfel R.** 2020. Virological assessment of hospitalized patients with COVID-2019. *Nature*:1-10
- Yu P, Zhu J, Zhang Z, Han Y, Huang L.** 2020. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. *Journal Infectious Diseases*
<http://dx.doi.org/10.1093/infdis/jiaa077>.
- Zhou F.** 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet* **395(10229)** 1054-1062.
[https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3).
- Zhou J.** 2014. Active replication of Middle East respiratory syndrome coronavirus and aberrant induction of inflammatory cytokines and chemokines in human macrophages: implications for pathogenesis. *The Journal of infectious diseases* **209**, 1331-1342.
- Zou L.** 2020. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *New England Journal of Medicine* **382**, 1177-1179.