REVIEW ARTICLE

COVID-19: A Worldwide, Zoonotic, Pandemic Outbreak

Tahseen Khan, MPharm; Kartikeya Agnihotri, BTech; Aditi Tripathi, BPharm; Suneet Mukherjee, BPharm; Namita Agnihotri, PhD; Gaurav Gupta, PhD

ABSTRACT

Context • An outbreak of a novel, zoonotic coronavirus occurred in December 2019 in the city of Wuhan, China and has now affected almost the entire world, with the maximum confirmed cases being 1 521 252 as of April 10, 2020. The WHO named this coronavirus 2019-nCoV, with COVID-19 being the name for diseases allied with it.

Objective • The study intended to examine the features and characteristics of existing human coronaviruses and identify their resemblance to the newly identified 2019-nCoV.

Design • The research team performed a literature review, searching relevant literature databases. We searched four databases, PubMed, EMBASE, Web of Science and CNKI (Chinese Database), to identify studies reporting COVID-19. Articles published on or before April 10, 2020 were eligible for inclusion. We used the following search terms: "Coronavirus" or "2019-nCoV" or "COVID-19" or "SARS-CoV" or "MERS-CoV" or "Bat SARS-CoV" or "ACE2 receptor".

Setting • This study was take place in School of Pharmacy, Suresh Gyan Vihar University, Jaipur, India.

Results • The undistinguishable similarity of the genomic sequences of Severe Respiratory Syndrome (SARS)-CoV, Middle East Respiratory Syndrome (MERS)-CoV, and Bat SARS-CoV—bat-SL-CoVZC45 and bat-SL-CoVZXC21—to nCoV-2019 has facilitated the process of identifying primary treatment measures. Researchers are presuming the existence of angiotensin-converting enzyme 2 (ACE2) receptor binding in nCoV-2019, as in SARS-CoV. Researchers have been examining human-to-human transmission, the possibility of an intermediate host between bats and humans, and the existence of asymptomatic cases. An incubation period of 0 to 14 days has been reported, with acute to chronic symptoms being cough, nasal congestion, high fever, dyspnea, pneumonia, invasive lesions in both lungs, respiratory failure, and even death, including in pediatric cases. Mechanical ventilation, extracorporeal membrane oxygenation, repurposing of antivirals, and plasma infusion have proven to be somewhat effective. Several countries have started clinical trials to evaluate the safety and effectiveness of some drugs, but the ability to vaccinate people with existing or new molecules will require time. Previously learned lessons from SARS and MERS have led some areas to be well equipped in terms of the ability to take speedy action.

Conclusions • First-level treatments include repurposing antivirals and antimalarials, and plasma infusion should help, but development of existing or new molecules into vaccines will take time. The unpredictable trajectory of this outbreak demands careful surveillance to monitor the situation, draw strategies, implement control measures, and create proper ethical laws and medical guidelines. (*Altern Ther Health Med.* 2020;26(S2):56-64)

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A retrospective analysis recently indicated that the first case of a coronavirus of unknown pneumonia etiology had been reported on December 12, 2019 and had been confirmed by the Wuhan Municipal health commission in Wuhan, Hubei, China, on December 31, 2019.[1,2] According to the Wall Street Journal on January 9, 2020, the Chinese Center for Disease Control and Prevention (CDC) confirmed that its causative agent is a third, zoonotic human coronavirus (CoV), provisionally named the 2019 novel coronavirus or 2019-nCoV.[3] On February 12, 2020, the World Health Organization (WHO) announced that the official name of the disease would be COVID-19. WHO's Director-General

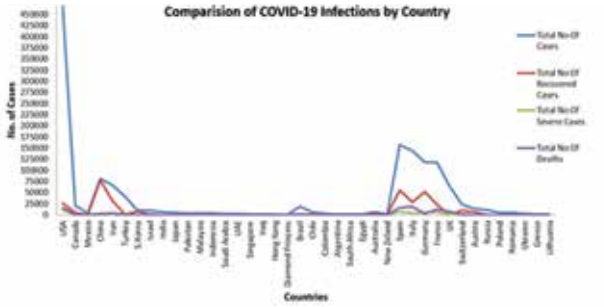
Table 1. Comparison of Total Number of Reported COVID-19 Cases by Country Through April 10, 2020.[9]

Country	Total Cases N	Total Recovered Cases n	Total Severe Cases n	Total Deaths n
USA	468 895	25 928	10 968	16 697
Spain	157 022	55 668	7371	15 843
Italy	143 626	28 470	3605	18 279
Germany	118 235	52 407	4895	2 607
France	117 749	23 206	7066	12 210
China	81 907	77 455	144	3336
Turkey	42 282	2142	1552	908
Iran	66 220	32 309	3918	4110
UK	65 077	135	1559	7978
Switzerland	24 172	10 600	386	958
Canada	20 765	5311	518	509
Brazil	18 176	173	296	957
Austria	13 377	6064	261	319
Russia	11 917	795	8	94
S. Korea	10 450	7117	55	208
Israel	10 095	1061	164	92
India	6771	635	0	228
Australia	6203	3141	74	53
Chile	5972	1274	360	57
Poland	5742	318	160	175
Japan	5530	685	109	99
Romania	5467	729	183	257
Pakistan	4601	727	45	66
Malaysia	4346	1830	69	70
Indonesia	3512	282	0	306
Mexico	3441	633	89	194
Saudi Arabia	3287	666	41	44
UAE	2990	268	1	14
Colombia	2223	174	85	69
Ukraine	2203	61	33	69
Greece	1955	269	79	87
South Africa	1934	95	7	18
Singapore	1910	460	29	6
Argentina	1894	365	96	79
Egypt	1699	348	0	118
New Zealand	1283	373	5	2
Iraq	1232	496	0	69
Lithuania	999	8	21	17
Hong Kong	990	309	15	4
Diamond Princess	691	17	36	3
Totals	**1 446 840**	**343 004**	**44 303**	**87 209**

Tedros Adhanom Ghebreyesus said that "the CO stands for Corona, the VI for virus, and the D for disease, and 19 stands for the year of initial occurrence of this lethal menace.[4,5]

In the initial cluster of patients, health officials found a connection to and exposure at a seafood market in Wuhan, indicating that the transmission source was from animal to human. With the extensive and rapid increase in the number of cases, Wuhan went on high alert for travelers, and the seafood market closed on January 01, 2020. The virus can be detected by genomic sequencing technology and by electron microscope.[6,7] A throat swab of patients provides the samples for testing.

Figure 1. Cases of COVID-19 Infection by Country Through April 10, 2020



The current literature review intended to examine the features and characteristics of existing human coronaviruses and identify their resemblance to the newly identified 2019-nCoV.

METHODS

Procedures

The research team searched the relevant literature databases. We searched four databases, PubMed, EMBASE, Web of Science and CNKI (Chinese Database), to identify studies reporting COVID-19. Articles published on or before April 10, 2020 were eligible for inclusion. We used the following search terms: "Coronavirus" or "2019-nCoV" or "COVID-19" or "SARS-CoV" or "MERS-CoV" or "Bat SARS-CoV" or "ACE2 receptor". References of all retrieved studies were screened for additional eligible publications. Primary studies were eligible if they reported any information on COVID-19 patients without restriction on study type or study design. We excluded studies that focused on infection in infants, did not report original data or clear diagnostic criteria, and no reliable clinical data.

Two independent reviewers screened the literature search and assessed each study for inclusion. Any disagreement was solved by consulting a senior investigator.

RESULTS

Epidemic Analysis

The outbreak began in Hubei province but hasn't been limited to China; it's also reached devastatingly into many other countries and almost into the entire world. The confirmed cases of COVID-19 worldwide through April 10, 2020 had reached 1,446,840.[8] Table 1 shows the total number of cases, the recovered cases, the severe cases, and the deaths in 40 countries through April 10, 2020, based on data collected by various studies.[9]

China was the first main region of infection, with the total number of cases reaching 81 907 as of April 10.[10] The USA, Spain, and Italy have had many more cases, reaching 468 895, 157 022, and 143 626 cases, respectively (Table 1).[11]

Figure 1 shows a comparison by country of the 4 categories of cases shown in the table. It clearly depicts the impact of the 2019-nCoV, not only in China but also in all other countries. Because its coverage is global, WHO has declared it to be a public health emergency.[12,13] Control measures have continuously been the topmost priority, with measures including keeping infected patients in isolation as

the initial treatment measure, in the absence of actual vaccination and medication.

To aid in the interpretation of the prevalence and spread of the virus, Table 2 and Figure 2 show the total daily confirmed cases for 21 days, in USA and Spain cases from March 21 to April 10, 2020 and in China and Japan from January 21 to February 22, 2020. They portray the effects, severity of infection, and impacts of the disease in the regions, which can help researchers, doctors, and governments of the respective regions to take appropriate control measures to overcome the spread of COVID-19.

Table 3 shows a comparison of the growth factor for the disease over 10 days, for the USA and Spain from April 01 to April 10, 2020 and for China and Japan from February 01 to February 10, 2020. The growth factor is the factor by which a quantity multiplies itself as calculated with the formula: growth factor = total number of daily cases / total number of cases on the previous day.[14,15]

The A value above 1 for the growth factor indicates an increase, whereas a value between 0 and 1 indicates a decrease in the rate. A growth factor value below 1—or above 1 but trending downward—is a positive sign, whereas a value constantly increasing above 1 is a sign of an exponential growth in the number of cases.

Figure 3 shows the largest variation occurring on February 8 between China and Japan, with a difference in value of 1.2518, which illustrates an increase in cases. This data provides a helpful insight into the spread of the virus.[16,17]

The mortality rate of COVID-19 has varied by nation and region, with WHO initially mentioning an estimated mortality rate of 2% as of January 29, 2020 and of 3.4% as of March 03, 2020. WHO has also mentioned that the fatality rate can't be confirmed until the end of the outbreak, and according to epidemiologists, as a virus undergoes mutation, the fatality rate can also change.[18]

Characteristics of Coronaviruses

A coronavirus is a large, enveloped, nonsegmented, positive-strand RNA virus, ranging from 26 to 32 kilobases (Kb) in length and 80 to 120 nanometers (nm) in diameter and belonging to family coronaviruses and the order Nidovirales.

The coronavirus membrane consists of at least 3 proteins, such as the spike (S) protein, membrane (M) protein, and envelope (E) protein. The helical capsid in the core forms when the RNA genome is complexed with nucleocapsid protein (N). An additional I protein encoded within the open reading frame (ORF) in the nucleocapsid belongs to the group II virion.

Coronaviruses are proficient in rapid mutation and recombination and are extensively distributed in innumerable avian hosts, mammals, and humans. Coronaviruses are classified into 4 genera: alphacoronavirus, betacoronavirus, deltacoronavirus, and gammacoronavirus. Alpha- and betacoronaviruses have gene sources from bats and are mainly found in

Table 2. Comparison of the Total Number of Confirmed COVID-19 Cases over 21 Days, for the USA and Spain from March 21 to April 10, 2020 and for China and Japan From January 21 to February 10, 2020

	Total Confirmed Cases			Total Confirmed Cases	
Dates	USA	Spain	Dates	Japan	China
March 21	15 219	19 980	January 21	0	282
March 22	15 219	24 926	January 22	1	309
March 23	31 573	28 572	January 23	1	571
March 24	42 164	33 089	January 24	1	830
March 25	51 914	39 673	January 25	3	1297
March 26	63 570	47 610	January 26	3	1985
March 27	68 334	56 188	January 27	4	2761
March 28	85 228	64 059	January 28	6	4537
March 29	103 321	72 248	January 29	7	5997
March 30	122 653	78 797	January 30	11	7736
March 31	140 640	85 195	January 31	14	9720
April 1	163 199	94 417	February 1	17	11 821
April 2	187 302	102 136	February 2	20	14 411
April 3	213 600	110 238	February 3	20	17 238
April 4	241 703	117 710	February 4	24	20 471
April 5	273 808	124 736	February 5	25	24 363
April 6	307 318	130 759	February 6	50	28 060
April 7	333 811	135 032	February 7	50	31 211
April 8	363 321	140 510	February 8	52	34 598
April 9	395 030	146 690	February 9	64	37 251
April 10	468 895	157 022	February 10	76	40 235

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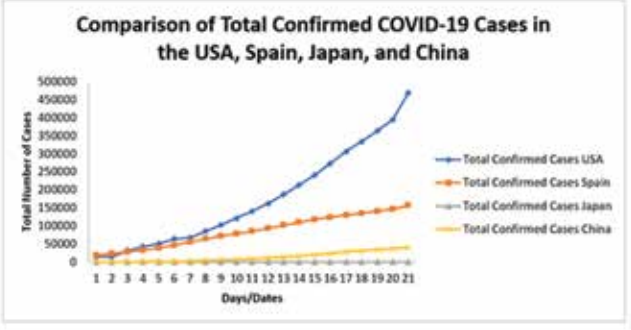

Table 3. Comparison of the Growth Factors for Reported COVID19 cases over 10 Days, for the USA and Spain From April 1 to April 10, 2020 and for China and Japan from February 1 to February 10, 2020.

	Growth Factor			Growth Factor	
Dates	USA	Spain	Dates	China	Japan
April 1	1.2541	1.4413	February 1	1.2242	1.2142
April 2	1.0684	0.837	February 2	1.0894	1.1764
April 3	1.091	1.0496	February 3	1.1416	1
April 4	1.0686	0.9222	February 4	1.2117	1.2
April 5	1.1424	0.9403	February 5	0.9485	1.0416
April 6	1.0437	0.8572	February 6	0.8495	1.04
April 7	0.7905	0.7094	February 7	1.0866	1.2692
April 8	1.1138	1.282	February 8	0.7785	2.0303
April 9	1.0745	1.1281	February 9	1.1214	1.4626
April 10	0.9731	0.9313	February 10	0.8483	1.051

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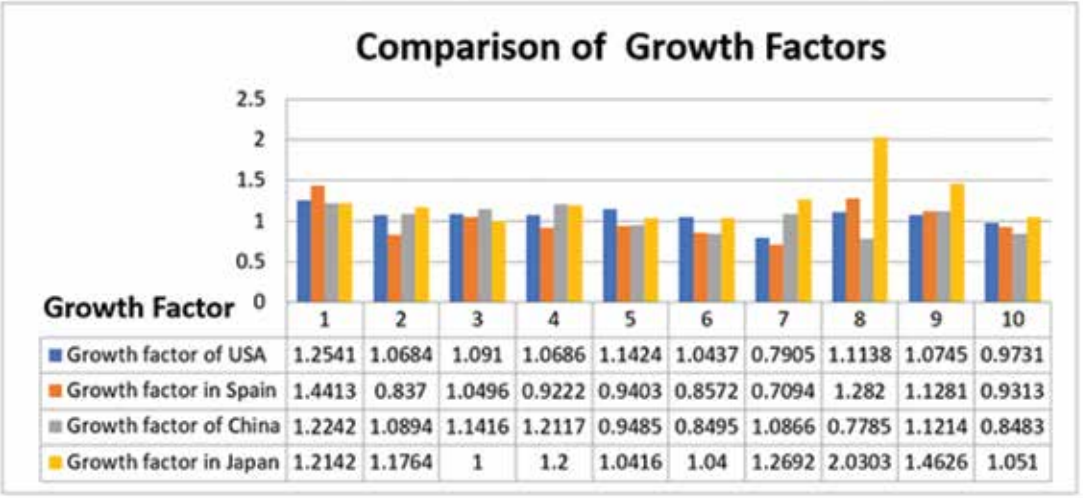


	1	2	3	4	5	6	7	8	9	10
Growth factor of USA	1.2541	1.0684	1.091	1.0686	1.1424	1.0437	0.7905	1.1138	1.0745	0.9731
Growth factor in Spain	1.4413	0.837	1.0496	0.9222	0.9403	0.8572	0.7094	1.282	1.1281	0.9313
Growth factor of China	1.2242	1.0894	1.1416	1.2117	0.9485	0.8495	1.0866	0.7785	1.1214	0.8483
Growth factor in Japan	1.2142	1.1764	1	1.2	1.0416	1.04	1.2692	2.0303	1.4626	1.051

mammals, such as rodents, camels, masked palm civets, mice, dogs, cats, and humans. Delta- and gammacoronaviruses have gene sources from birds.

Currently, 7 strains of known human-transmitting coronaviruses are known, with the Wuhan coronavirus being the seventh, including[19,20]: (1) the human CoV 229E, (2) the human CoV OC43, (3) the Severe Respiratory Syndrome (SARS) CoV, (4) the human CoV NL63 or New Haven CoV, (5) the human CoV HKU1, (6) the Middle East Respiratory Syndrome (MERS) CoV, and (7) the 2019-novel coronavirus nCoV-2019.

CoV symptoms are generally mild and pathogenic clinically, causing mild upper respiratory disease, with the exception of SARS and MERS, which are 2 betacoronaviruses that infect humans and can cause major epidemics.

Resemblance of SARS-CoV and MERS-CoV to 2019-nCoV

Biomedical scientists are initiating countermeasure development for 2019-nCoV using SARS CoV and MERS CoV as prototype. This is because its genomic sequencing resembled to 2019-nCoV. The2019-nCoV belongs to 2B group is distinguished by arranging nucleotide arrangements and noticed distinct from SARS coronavirus strain. Some studies have also examined the whole genome of nCoV-2019 and found it to be approximately 80% identical to the original SARS-CoV.[21] Another study has also shown that the bat CoV's sequencing is 92% identical to that of 2019-nCoV.[22,23]

SARS-CoV. This CoV has been identified in bats, which act as a host. Several bat coronaviruses are genetically similar to human SARS CoV. These bat SARS-CoV form unique clade under the subgenus Sarbecovirus.

SARS-CoV arose in Foshan, Guangdong, Southern China, on November 16, 2002 and has resulted in more than 8098 human infections, 774 deaths in 37 countries during 2002 and 2003, and a mortality rate of 10% in the past 2 decades.[24] The resulting cost to the global economy has been predicted to be between $30 and $100 billion.[25]

The last human-to-human transmission was identified in China on May 18, 2004, and WHO has confirmed its control but has issued biosafety-concern guidelines.[26] The symptoms are cough, dyspnea, and diarrhea, and research has indicated that the spread is due to the binding of the SARS glycoprotein to the angiotensin-converting enzyme 2 (ACE2) in the human lower respiratory tract.[27-29]

MERS-CoV. This CoV was first spotted in Saudi Arabia in 2012, with the dromedary camel being a reservoir and the mode of transmission being from camel and camel, camel to human, and human to human.[30] It is a zoonotic virus allied with illness ranging from asymptomatic to mild upper respiratory distress to severe respiratory distress and even death. About 2494 laboratory confirmed cases of infection and 858 fatalities since September, 2012 and 38 death cases.[31] On December 05, 2019, the International Health Regulations (IHR) focal point for Qatar reported 3 laboratory-confirmed cases to WHO, which that organization confirmed on December 26, 2019.[32,33]

Mowbray revealed in 2012 that the sputum of a Saudi man, who died from respiratory failure, contained the MERS-CoV.[34] Mowbray indicated that the CoV had a prominent GI effect and could cause acute kidney failure due to the binding of the MERS-CoV glycoprotein to dipeptidyl peptidase 4 (DPP4) in the lower respiratory and gastrointestinal tracts and the kidney.[35]

Preliminary Efforts

At the current time, researchers are working hard to find the cause, symptoms, mechanisms of and the precautions, and treatments for COVID-19 by studying the genomic sequencing RT PCR (cov 5, cov 13). The betacoronavirus 2019-nCoV belongs to the family coronavirdae, the subfamily orthocoronavirinae, and the subfamily sarbecovirus.

Zhu et al have described the structural features of 2019-nCoV through electron microscopy using negatively stained particles.[36] The researchers indicate that the particles

are spherical and elliptical in shape with some pleomorphism, are about 60 to 140 nm in diameter, have distinct spikes of about 9 to 12 nm, and have been found in in the cytoplasm of membrane vesicles in an ultrathin section of human-airway epithelial tissue. Several studies have found the original host to be the bat, with transmittance to humans through some intermediate animal host (Figure 4).[37-39]

Using next-generation sequencing, Jasper et al have reported a phylogenetic analysis of 5 patients' RT-PCR amplicons and identified 2 full genomes; the data found a close relationship between COVID-19 and bat SARS-CoV (cov11) from Chinese horseshoe bats.[40]

Roujian Lu et al described that 2019- nCoV satisfactorily differing from SARS-CoV.[41] The researchers identified 10 genome sequences of 2019-nCoV from 9 patients and found them to be: (1) 99.98% identical to each other, (2) 88% identical to 2 bat SARS-CoVs—bat-SL-CoVZC45 and bat-SL-CoVZXC21, (3) about 79% identical to SARS-CoV, and (4) about 50% identical to MERS-CoV (Cov 4). Some other studies have reported 86% to 89% identicality to bat SAR-CoV. Figure 5 shows the genomic sequencing of Bat SARS-CoV and SARS-CoV.[42,43]

In a structural analysis, Benvenuto et al described the mutation of the surface protein nucleocapsid (Protein N) and Spike-like nucleoprotein (Protein S), which provide stability to the viral particle of 2019-nCov. The researchers explained that Protein S is responsible for the entry of the virus into the cell, which then binds to the ACE2 receptor, with continued fusion of the membrane. Protein N helps in the formation of the replicase complex and in the efficiency of the mounting virion assembly by viral transcription. This study confirmed substantial resemblance of 2019-nCov to bat-like SARS-CoV and less resemblance to SARS-CoV. Thus, 2019-nCov is less pathogenic than SARS-CoV but more than bat-like SARS-CoV.[44, 45]

ACE2 has been found to be the cell receptor for SARS-CoV,[27-29] providing another approach to determining its resemblance to 2019-nCov. Zhou et al's study confirmed ACE2 as a cell receptor for entry but indicated that no other coronavirus receptors used it, such as aminopeptidase N and DPP4.[46] Some studies have shown through phylogenetic analysis of the whole sequenced genome—the RNA-dependent RNA polymerase (RdRp) region and S-gene sequences—that 2019-nCov is 92.6% identical to Bat-CoVRaTG13, found in Rhinolophus affinis, and is a distinct lineage with less than an 80% proximity to 2019-nCoV.[47-50]

IgG and IgM ELISA test for bat SARS-CoV RP3 nucleocapsid protein showed 92% amino acid and 75% SARS-CoV amino acid identical to 2019-nCoV with no cross reactivity in contradiction of other coronaviruses excluding SARS-CoV. Nucleotide sequences of spike protein on the envelope of the virus is also exceedingly related with that of bat-SL-COVZC45 (84%) and SAR-Cov (78%). Based on these studies, a hypothetical diagrammatic representation of pathogenesis is explained in Figure 6.

Figure 4. Transmission of COVID-19 and Primary Treatment Approaches

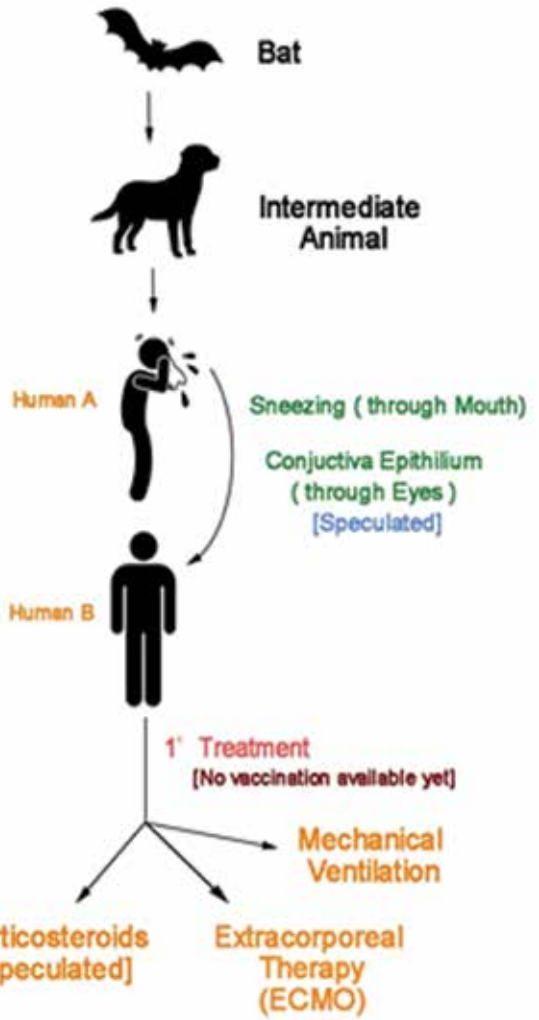
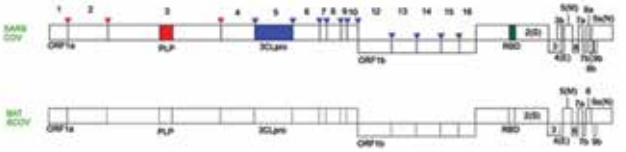


Figure 5. Genomic Sequencing of SARS-CoV and Bat SARS-CoV

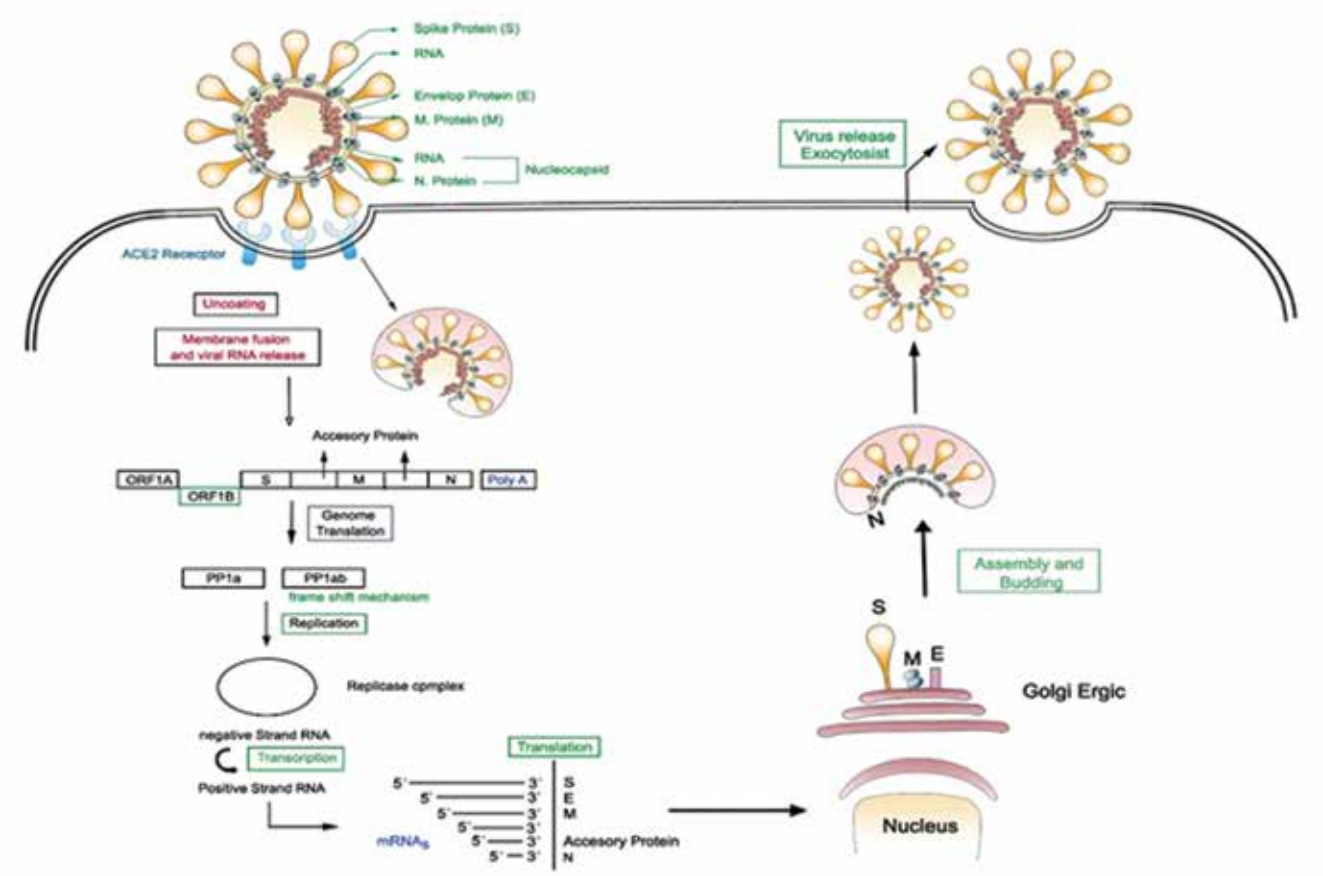


Abbreviations: SARS-CoV, Severe Respiratory Syndrome; ORF, open reading frame.

Transmission of COVID-19

Various studies have found that the transmission of COVID-19 can be human to human. Infection in medical workers and family clusters have confirmed the human-to-human infection as does that in 15 healthcare practitioners in Wuhan, China.[51] Transmission has taken place through the respiratory tract via coughing, sneezes, and talking loudly,

Figure 6. Hypothetical Mechanism and Pathogenesis of COVID-19. The spike protein of the virus binds to the ACE2 receptor at the binding site, uncoating and releasing the RNA. It undergoes genomic translation to form replicase complex and cause transcription from negative- to positive-strand RNA, which is associated with assembly and budding of virion and release through exocytosis.



Abbreviations: ACE2, angiotensin-converting enzyme 2; ORF, open reading frame.

and through close contact with the mouth and nose,[52] but transmission through breast milk from mother to infant has not yet been reported. Although not confirmed yet, a risk may exist for pregnant women in the vertical transmission from mother to baby; some studies are testing samples from nasopharyngeal swab of neonates, amniotic fluid, cord blood, and breastmilk. As of now, 2 neonatal COVID-19 cases have occurred, one 17 days after birth and other at 36 hours after birth, which might suggest transmission due to close contact and no evidence of vertical transmission.[53,54]

However, bit controversial but further studies are into consideration and surveillance for asymptomatic transmission. A case of asymptomatic transmission had been observed in the examination of 5 patients of a family cluster who returned to Shenzhen from Wuhan, China.[55] Another relevant case of asymptomatic transmission has been reported by Rothe et al in Germany, with a 33-year-old woman transmitting it to a German businessman.[56]

While it's not yet clear, some researchers have suggested that transmission through a fecal-oral route is possible because the virus has been found in the loose stool of patients in the USA.[57] Another suggestion is that transmission through the eyes may also be possible. Transmission has been detected in patients with COVID-19 who have worn masks to avoid respiratory tract transmission but have not protected their eyes.[58] Human conjunctival epithelium is vulnerable to infections via infectious droplets, such as through sneezes, and this fact may be one of the reasons for transmission.[34,59,60]

Incubation Period for 2019-nCoV

Determination of the incubation period for 2019-nCoV is challenging, and studies have shown different figures; WHO indicated a period ranging from 0 to 14 days.[61] whereas the European Center for Disease Control and Prevention (ECDC) indicated from 2 to 12 days.[62] Chan et al reported that symptoms were observed after 3 to 6 days. It is estimated that the mean incubation period for 2019-nCoV is 6.4 days.[63]

Symptoms of COVID-19

Various symptoms have been observed at different time intervals from onset to severe conditions. Most infected patients in the early stages have myalgia/ fatigue, cough, nasal

congestion, running nose, sputum production, high fever, malaise and restlessness, and poor appetite. The disease worsens later, with patients experiencing dyspnea, cyanosis, hemoptysis, leucopenia, lymphopenia, hypoxemia, acute kidney and cardiac injury, nosocomial pneumonia or bacteremia, metabolic acidosis, invasive lesions in both lungs, respiratory failure due to alveolar damage as shown in radiographic chest CT images, septic shock, irreversible bleeding, coagulation dysfunction, and even death. One study reported that 26 patients who previously had had substantial health conditions such as hypertension, diabetes, health or kidney issues, were found to be susceptible to 2019-nCoV.[64]

Primary Treatment Approaches

Doctors acknowledge that they are continuously trying new approaches for primary treatment of patients with mild-to-moderate, acute respiratory failure. As the method of spread is unclear, medical practitioners work first to avoid the spread and are implementing mechanical ventilation and extracorporeal membrane oxygenation. With the findings of the resemblance of COVID-19 to SARS and MERS, medications developed for them are now being used against COVID-19, including broad-spectrum antivirals, such as remdesivir, an RNA polymerase inhibitor; lopinavir; ritonavir; and interferon-beta. Many suggestions have been made for the use of antimalarial drugs such as hydroxychloroquine or chloroquine for COVID 19 patients and severe pneumonia.

The use of corticosteroids for COVID-19 lung injury provided some controversial and mixed reviews. Russell et al recommend not to use corticosteroids except in clinical trials,[65] whereas some other studies are supporting its use.[66] Chen et al in a SARS study observed positive results in mortality reduction when corticosteroids were given to 401 patients.[6] Experts have proposed some precautionary measures to take before giving corticosteroids, such as checking some factors depending on a disease's severity, with a low-to-moderate doses for short durations being suggested—≤0·5–1 mg/kg per day of methylprednisolone or the equivalent ≤7 days—and cautious use in patients with previously and regular corticosteroid intake and with hypoxemia.[67,68]

On February 16, 2020, China's regulatory body, the National Medical Products Administration, approved an antiviral drug, Favilavir, (Zhejiang Hisun Pharmaceuticals) for marketing because it had shown therapeutic efficacy for COVID-19. Clinical trials on 70 patients in Shenzhen, Guangdong province demonstrated its effectiveness with minor side effects.[69,70] A generic version of Favilavir received approval.

On February 17, 2020, the National Health Commission of China provided a brief about the use of convalescent plasma therapy. Plasma infusion has been identified as a ray of hope for critically ill patients with COVID-19. Infusion of the plasma of recovered patients, who have developed specific antibodies against the virus, has been found to improve clinical symptoms and be effective in recovery from COVID-19. Zhang Dingyu, head of Wuhan Jinyintan Hospital, has reported the discharge of one recovered patient among 11 patients who had been given the plasma treatment.[67,68,71-73]

One study published as a preprint suggested the effectiveness of tocilizumab, an anti-IL-6 receptor drug, for severely ill COVID-19 patients. The National Institutes of Health has approved a clinical trial of hydroxychloroquine to evaluate the safety and efficacy of COVID-19 for patients.[74,75]

The fight against COVID-19 is causing researchers to widen their horizons. Many countries have begun clinical trials, such as a clinical trial that the University of Oxford, UK, has initiated, called Recovery, to assess different drugs.[76] The drugs include the HIV drugs lopinavir and ritonavir and the anti-inflammatory drug dexamethasone, as potential treatments for hospitalized COVID-19 patients.

The Montreal Heart Institute's Research Center in Canada has started a clinical trial, Colcorona,[77] to assess whether short-term treatment with colchicine reduces the rate of death and lung complications related to COVID-19. Approximately 6000 patients will be enrolled to receive either colchicine or placebo (1:1 allocation ratio) for 30 days. Follow-up assessments will occur at 15 and 30 days following randomization for evaluation of the occurrence of any trial endpoints or other adverse events.

Another study is Inserm, a clinical trial called Discovery, that a French firm has initiated on 4 investigational therapies in a minimum of 800 severely ill patients with COVID-19 in France.[78-80] It's expected to enroll approximately 3200 participants across Belgium, Germany, Luxembourg, the Netherlands, Spain, Sweden, and the UK. The study will evaluate remdesivir, lopinavir, and ritonavir in combination, where the latter is being administered with or without hydroxychloroquine or interferon beta.

CONCLUSIONS

COVID-19 has increased the load on researchers, drug makers, and governments, but their prompt actions and sincerity have been commendable. Governments should focus on boosting the immunity of individuals because it plays an important role in combatting these viral infections, hence it's urgently required to develop a vaccine. First-level treatments include repurposing antivirals and antimalarials, and plasma infusion should help, but development of existing or new molecules into vaccines will take time. The unpredictable trajectory of this outbreak demands careful surveillance to monitor the situation, draw strategies, implement control measures, and create proper ethical laws and medical guidelines.

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