Review Article

COVID-19: Major Pandemic of the Millennium

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ABSTRACT

A previous unidentified coronavirus, currently referred to as the 2019 novel coronavirus, originated from Wuhan, China in late December 2019, resulting in a formidable outbreak in many Chinese cities and spreading worldwide. The disease is formally known as Coronavirus Disease-2019 (COVID-19, February 11, 2020, by WHO). Coronaviruses (CoVs) are a wide family of single stranded, enveloped, zoonotic RNA viruses. Corona virus causes respiratory infections including pneumonia, vomiting, sneezing and coughing while diarrhea and upper respiratory diseases occur in animals. The corona virus was transmitted by airborne droplets to humans or humans to animals. Corona virus enters human cell through exopeptidase receptor ACE-2 membrane. Thus, the production of new CoV therapies as well as vaccinations are urgently required to help mitigate the spread of the virus from infected patients, thus minimizing the risk of any possible pandemic. Our main goals are to highlight and describe the current knowledge about corona virus.

Keywords: Coronavirus COVID-19; Pneumonia; Respiratory Infection, MERS-CoV, SARS-CoV.

INTRODUCTION

Coronavirus is an enveloped, positive single-strand RNA virus. It belongs to the Orthocoronavirinae subfamily, as the name, with the characteristic "crown-like" spikes on their surfaces.[1] Bat SARS-like CoV and others also fall within the beta-coronavirus genus along with SARS-CoV. COVID-19 (caused by 2019-nCoV infection) is listed as a communicable disease of fifth grade in Taiwan on 15 January 2019.[2] The beta-coronavirus genus can be broken down into many subgroups. Sarbecovirus belongs to the 2019-nCoV, SARS-CoV, and bat SARS-like CoV, while MERS-CoV belongs to Merbecovirus.[3] SARSCoV, MERS-CoV, and 2019-nCoV all cause disease in humans but each subgroup may have slightly different biological characteristics and virulence.[1,4,5]

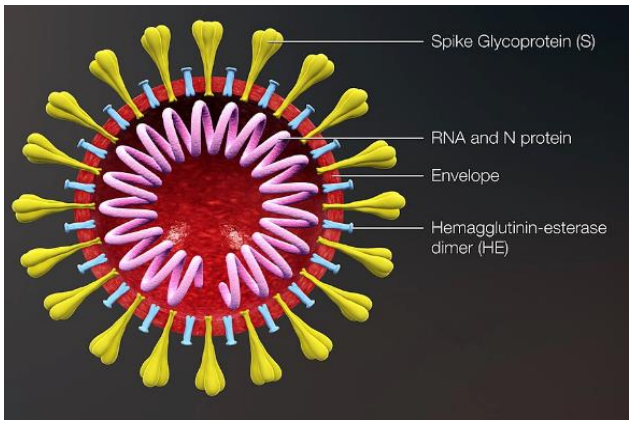

Figure 1: Structure of coronavirus

HISTORY AND ORIGIN

In 1960 the first case of corona virus was identified as cold. Roughly 500 patients have been classified as flu-like systems, according to the 2001 Canadian report.[17-18] cases of these were reported as polymerase chain reaction infected with corona virus strain. Until 2002 Corona was treated as a common non-fatal virus. In 2003, numerous studies were released with proofs of spreading the corona to several countries such as USA, Hong Kong, Singapore, Thailand, Vietnam and Taiwan. Many cases of extreme acute respiratory syndrome caused by corona were recorded in 2003, and their mortally over 1000 patient. To a microbiologist this has been the black year. Then the search was initiated for microbiologists to understand these issues. They conclude and understand the pathogenesis of the disease after an in-depth exercise and discovered it as a corona virus. But up to the total of 8096 patients were confirmed as having corona virus infection.

Therefore, in 2004, the World Health Organization and disease control and prevention centers declared a "state emergency". Another Hong Kong research report reported 50 patients with extreme acute respiratory syndrome and 30 of them were found to be infected with corona virus. Several infected patients and deaths were reported in Saudi Arabia in 2012.[6–9] COVID-19 was first detected and isolated from the patent on pneumonia belongs to Wuhan, China.[10–11] The exact origin, location, and natural reservoir of the 2019-nCoV remain unknown, although the virus is assumed to be zoonotic and bats may be the culprits due to sequence similarity with the bat-CoV.[1,3]

Table 1: Chronological list of Covid-19 global outbreak

S. No.	Date	Events
1	November, 2019	Mysterious pneumonia in Wuhan, Hubei, China
2	1 December, 2019	The first confirmed nCoV case in Wuhan (no Huanan seafood market exposure)
3	10 December, 2019	The first confirmed nCoV case with Huanan seafood market exposure
4	31 December, 2020	An epidemiological alert by local agency
5	1 January, 2020	Huanan seafood market shut down
6	13 January, 2020	The first nCoV case in Thailand (Wuhan history)
7	15 January, 2020	A notifiable communicable disease (by Taiwan CDC)
8	21 January, 2020	The first nCoV case in Taiwan (Wuhan history)
9	30 January, 2020	Public health emergencies of international concern (PHEIC) alarm by WHO
10	3 February, 2020	WHO releases the international community's Strategic Preparedness and Response Plan to help protect states with weaker health systems
11	11 March, 2020	The WHO officially declared it a pandemic
12	18 March, 2020	WHO and partners launch the Solidarity Trial, an international clinical trial that aims to generate robust data from around the world to find the most effective treatments for COVID-19.

HUMAN CORONAVIRUS TYPES

The coronaviruses on their surface are named for the crown-like spikes. There are four main coronavirus subgroupings, called alpha, beta, gamma, and delta. The seven coronaviruses which can infect humans are:

Common human coronaviruses

1. 229E (alpha coronavirus)

2. NL63 (alpha coronavirus)

3. OC43 (beta coronavirus)

4. HKU1 (beta coronavirus)

Other human coronaviruses

5. MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)

6. SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS)

7. SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19)[12]

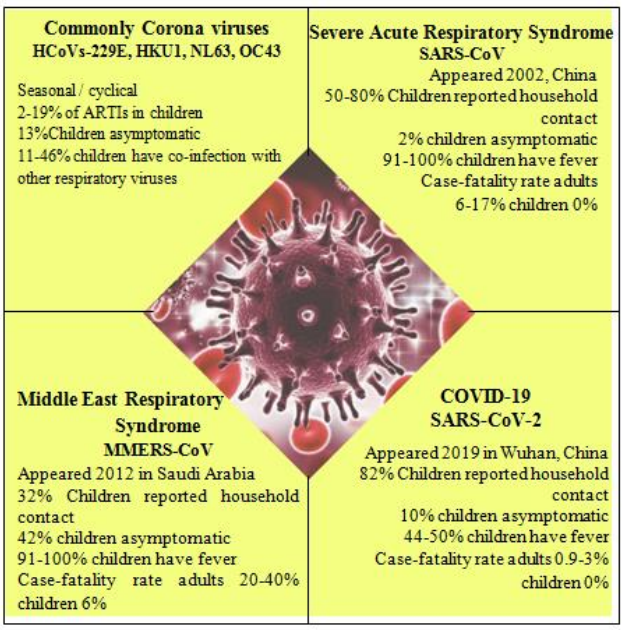

Figure 2: Summary of coronavirus diseases. COVID-19 indicates coronavirus disease 2019

Characteristics

According to a study published on 24 January 2020, patients diagnosed with corona virus have many common characteristics, such as fever, cough, and fatigue, though diarrhea and dyspnea have been found to be as rare. Many of them reported bilateral abnormalities as being patient. In 2020, corona virus was isolated in china from bronchoalvelor lavage fluid. It's also present in blood samples. Until now, corona virus has not been confirmed in proprietary feasts and urine samples.[13–15]

MODES OF TRANSMISSION OF THE COVID-19 VIRUS

Respiratory infections can be transmitted by droplets of different sizes: if the droplet particles are > 5-10 µm in diameter, they are referred to as respiratory droplets and < 5 µm in diameter, they are referred to as droplet nuclei.[16] According to current evidence, COVID-19 virus is transmitted primarily between people through respiratory droplets and contact routes.[17-22] In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported.[23]

Droplet transmission occurs when a person is in close contact (within 1 m) with someone who has respiratory symptoms (e.g., coughing or sneezing) and is thus at risk of exposure to potentially infectious respiratory droplets through his / her mucosa (mouth and nose) or conjunctive (eyes). In the immediate environment, transmission can also occur via fomites around the infected person.[23] Consequently, COVID-19 virus transmission can occur through direct contact with infected people and indirect contact with surfaces in the immediate environment or with items used on the infected person (e.g., stethoscope or thermometer).

Airborne transmission is distinct from droplet transmission as it refers to the presence of microbes within droplet nuclei, which are usually called particles < 5µm in diameter, can stay in the air for long periods of time, and can be transmitted to others over distances greater than 1 m.

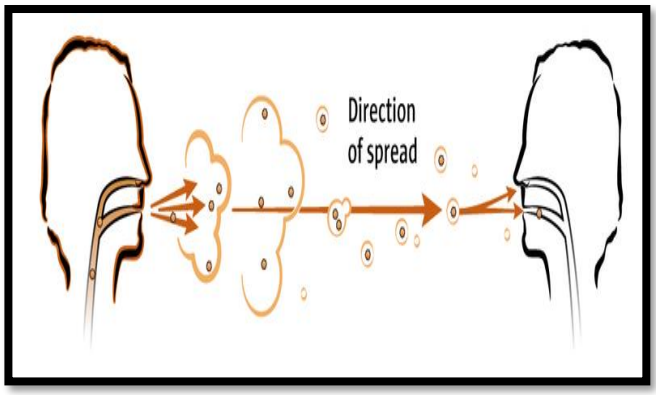

Figure 3: Transmission of corona virus via airborne droplets.

In the context of COVID-19, airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed; i.e., endotracheal intubation, bronchoscopy, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation.

There is some evidence that infection with COVID-19 can lead to bowel infection and can be found in faeces. To date, however, only one study has cultured the COVID-19 virus from a single stool specimen.[24] Hitherto, there have been no records of COVID-19 virus faecal-oral transmission.

SYMPTOMS

The most common COVID-19 symptoms are fever, dry cough and tiredness. Some patients may experience pain and aches, nasal congestion, sore throat or diarrhea. Typically these symptoms are mild, and start slowly. Many people get sick but have only very mild symptoms. Most people (around 80 percent) recover from the disease without needing treatment in hospital. About 1 in every 5 people who get COVID-19 get seriously ill and develop breathing difficulties. Older people, and those with underlying medical issues such as high blood pressure, heart and lung problems, diabetes or cancer, are at higher risk of developing severe illness. Someone can catch COVID-19 however and get seriously ill. Even people with very mild COVID-19 symptoms may be transmitting the virus. Persons of all ages suffering fever, cough and breathing problems should seek medical attention.[25]

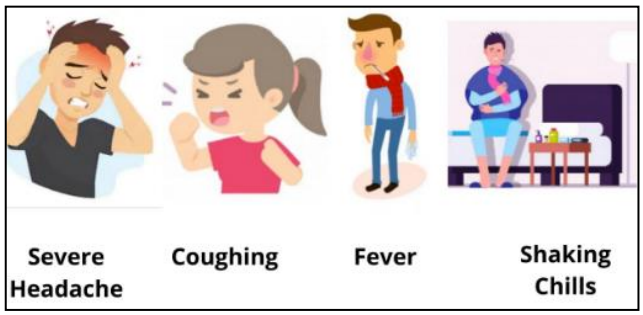

Figure 4: Symptoms of covid-19

DIAGNOSIS

Real-time polymerase chain reaction (RT-PCR) on upper or lower respiratory secretions is the principal basis for diagnosing HCoV infections. [26-32] Higher viral loads were found in samples from the lower respiratory tract compared to the upper respiratory tract for SARS-CoV, MERS-CoV and SARS-CoV-2.[35,36]

Therefore, additional testing of the upper respiratory tract samples or (preferably) testing of the lower respiratory tract samples should be performed in clinically suspicious cases with an initially negative result on nasopharyngeal or throat swab. RT-PCRs may be positive for HCoVs on stool samples but are not used for routine diagnosis.[29, 37, 38] Rare cases of positive PCRs in the blood have been identified in SARS-CoV and SARS-CoV-2.[35, 39] Serology has been used for the diagnosis of SARS-CoV and MERS-CoV infections but is not useful in the acute infection stage.[40-42] Cross-reactivities have been observed between SARS-CoV antibodies and can CoVs.[43]

TREATMENT

COVID-19 actually does not have an approved therapy. The key techniques are symptomatic and supportive treatment, such as holding vital signs, maintaining blood pressure and oxygen saturation, and managing complications, such as secondary infections or failure of organs. Because of COVID-19's possible mortality several medical treatments are underway:

1. Convalescent therapies (plasma from recovered COVID-19 patients): This technique was used to promote passive vaccination. Based on MERS reports, therapeutic agents with potential benefits include convalescent plasma, interferon-beta / ribavirin combination therapy, and lopinavir.[44] However, COVID-19 has no experience and no randomized controlled clinical trials are currently underway for this treatment.

2. Vaccine: There is currently no effective vaccine to prevent an infection with 2019-nCoV. The spike protein may serve as a candidate for vaccine, but the effect on humans needs further assessment[45].

3. Potential drugs: Several studies have suggested medicines which are potentially useful for COVID-19 treatment (Table 2). Most of these suggestions are based on in vitro trials, virtual screenings and recordings of their SARS and MERS effects.

Table 2: Potential drugs for COVID-19[65]

S. No.	Drug	Method	Mechanism of action	References
1	Atazanavir Efavirenz Ritonavir Dolutegravir	Molecule Transformer-Drug Target Interaction (MT-DTI)	Binding to SARS-CoV-2 3C-like proteinase (3CLp r o)	Beck *et al.,* 2020 (46)
2	Angiotensin converting enzyme inhibitors and Angiotensin1 receptor inhibitors	Brief review	Rebalancing Renin-Angiotensin-Aldosterone System (RAAS) (might reduce the pulmonary inflammatory response and mortality)	Sun *et al.,* 2020 (47)
3	(Angiotensin II human acetate) GHRP-2 Indinavir Cobicistat Caspofungin acetate Lopinavir, Atazanavir	Virtual screening	Binding to SARS-CoV-2 Mp r o: Angiotensin II human acetate, GHRP-2, Indinavir, and Cobicistat Binding to SARS-CoV-2 3C-like proteinase (3CLp r o): Angiotensin II human acetate, GHRP-2, Indinavir, Caspofungin acetate, Lopinavir, and Atazanavir	Contini *et al.,* 2020 (48)
4	Beclabuvir Saquinavir	Virtual screening	Binding to SARS-CoV-2Mp r o	Sekhar *et al.,* 2020 (49)
5	Baricitinib	Using Benevolent AI	Binding to AP2-associated protein kinase 1 (AAK1)	Richardson *et al.,* 2020 (50)
6	Chloroquine Remdesivir	*In vitro* study	Reducing viral copy numbers in the cell supernatant and viral infection	Wang *et al.,* 2020 (51)
7	Colistin Valrubicin Icatibant Bepotastine Epirubicin Epoprostenol Vapreotide Aprepitant, Caspofungin perphenazine	Virtual screening	Binding to SARS-CoV-2Mp r o	Liu *et al.,* 2020 (52)
8	Carfilzomib Eravacycline Valrubicin, Lopinavir Elbasvir Streptomycin	Virtual screening	Binding to SARS-CoV-2 protease	Wang *et al.,* 2020 (53)
9	Ebselen	Virtual screening	Binding to SARS-CoV-2Mp r o	Jin *et al.,* 2020 (54)
10	Eriodictyol Isoniazid pyruvate Nitrofurantoin Cepharanthine Ergoloid Hypericin	Virtual screening	Binding potency to Viral S-protein at its host receptor region or to the S protein-human ACE2 interface	Smith *et al.,* 2020 (55)
11	Formoterol Chloroquine	Virtual screening	Binding to SARS-CoV-2 papainlike protease (PLp r o)	Arya *et al.,* 2020 (56)
12	Ikarugamycin molsidomine	Connectivity map (Cmap)	Effective on the genes coexpressed with ACE2	Li *et al.,* 2020 (57)
13	Ledipasvir velpatasvir	virtual screening	Binding to SARS-CoV-2 3C-like proteinase (3CLp r o)	Chen *et al.,* 2020 (58)
14	Lithium	Brief review	Probably by reducing apoptosis and inhibition of glycogen synthase kinase 3 beta (GSK-3^{-})	Nowak *et al.,* 2020 (59)
15	Mycophenolic acid Grazoprevir Telaprevir Boceprevir	Virtual screening	Binding to SARS-CoV-2 papainlike protease (PLp r o)	Elfiky *et al.,* 2020 (60)
16	Nelfinavir	Virtual screening	Binding to SARS-CoV-2Mp r o	Xu *et al.,* 2020 (61)
17	Rupintrivir Lopinavir Remdesivir Binding to	Virtual screening	SARS-CoV-2Mp r o	Shang *et al.,* 2020 (62)
18	Teicoplanin	In vitro study	Preventing the entrance of SARSCoV- 2-Spike-pseudoviruses into the cytoplasm	Zhang *et al.,* 2020 (63)
19	Thymopentin Carfilzomib Saquinavir	Virtual screening	Binding to SARS-CoV-2 3C-like proteinase (3CLp r o)	Wang *et al.,* 2020 (64)

PREVENTION

Since there are no standard COVID-19 treatments, it's necessary to prevent infection or spreading further. Travel to COVID-19 epidemic region, touch, or consuming wild animals is dissuaded for general population. For those who have travel history from an outbreak area in the last 14 days, body temperature tracking and self-monitoring should be carried out for 14 days.

If compatible symptoms arise, it is recommended that transport be assigned to avoid unsafe exposure. Personal protective equipment should be placed on and removed correctly for health-care staff when caring for a likely or confirmed patient. Strict safety protocols for high-risk protocols (such as endoscopy, Ambu bagging, and intubation with the endotracheal tube) should be carried out. Once exposed to blood or body fluids of the patient unprotected, the healthcare workers should flush thoroughly the exposure site by water or soap. Body temperatures should be tracked for 14 days afterwards. The confirmed case should be isolated (prefer an insulating space with negative pressure or, preferably, a single room with good ventilation). Isolation can be allowed under the conditions of resolved symptoms for 24 hours and consecutive two negative outcomes. Deep burning or burial of bodies should be done.

Treatments effective against coronavirus include steam and heat. The virus is susceptible to other active ingredients (AIs), such as sodium hypochlorite (0.1% –0.5%), 70% ethyl alcohol, povidone-iodine (1% iodine), chloroxylenol (0.24%), 50% isopropanol, 0.05% benzalconium chloride, 1% cresol soap, or hydrogen peroxide (0.5% –7.0%), etc. Just like the WHO recommendations for Ebola virus (RG4) disinfection, the environment with spills of blood or body fluids could be cleaned up with 1:10 dilution of 5.25% household bleach for 10 minutes.[66]

CONCLUSION

Covid-19 is a new virus epidemic which has challenged World's cultural, health and public health infrastructure. Time alone can say how this virus affects our lives here in India. There is actually no specific cure for the condition, and the only method is supportive care. While there are several experimental trials on the way, the most we can do to avoid an epidemic outbreak is strict surgery to manage infection. First-line health care professionals will be very aware of effective steps for the prevention of infections for suspicious patients.

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