



Comprehensive update on current outbreak of novel coronavirus infection (2019-nCoV)

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Abstract: Recently, a new coronavirus disease (COVID-19) has emerged as a respiratory infection with significant concern for global public health hazards. With an initial suspicion of the animal to the human transmission for earlier cases, now the paradigm has shifted towards human to human transmission via droplets, contacts and/or through fomites. With each passing day, more and more confirmed cases are being reported worldwide which has alarmed the global authorities including World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and the National Health Commission of the People's Republic of China to take immediate action in order to reduce the transmission and subsequent mortalities associated with COVID-19 to as minimum as possible. Unfortunately, like the previous Coronavirus outbreaks, there is no definite antiviral therapy for the treatment of confirmed cases and hence preventing ourselves from contracting 2019-nCoV is the best way to prevent it from becoming pandemic. Herein, we aim to discuss the latest updates on the origin, genomic characteristics, diagnosis, treatment options and current efforts being made by international health organizations with regards to the 2019-nCoV outbreak.

Keywords: Respiratory disease; viral infection; coronavirus; World Health Organization; quarantine period

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Introduction

Recently, a new coronavirus strain has become a matter of concern for human lives (1). Since the beginning of 21st Century, the current coronavirus outbreak is the third coronavirus attack, the previous one being Severe acute respiratory syndrome-related coronavirus (SARS-CoV) epidemic [2003] and Middle East respiratory syndrome coronavirus (MERS-CoV) epidemic [2012] (Figure 1). On 31 December 2019, clusters of acute respiratory illness cases were reported among people associated with the Hunan seafood and animal market in the city of Wuhan, China. Within 1 month of reporting of novel coronavirus associated acute respiratory illness, more than 70,000 confirmed cases

have been reported with a reported mortality of around 2% to 3% in these patients (2-4). This outbreak also seems to be challenging to manage just like the previous coronavirus outbreaks considering the rapid spread via droplets and non availability of any effective vaccines or antiviral drugs.

Epidemiology

Demographic spread

Recently, a new coronavirus strain has become a matter of concern for human lives (1). Since the beginning of the 21st Century, the current coronavirus outbreak is the third coronavirus attack, the previous one being Severe

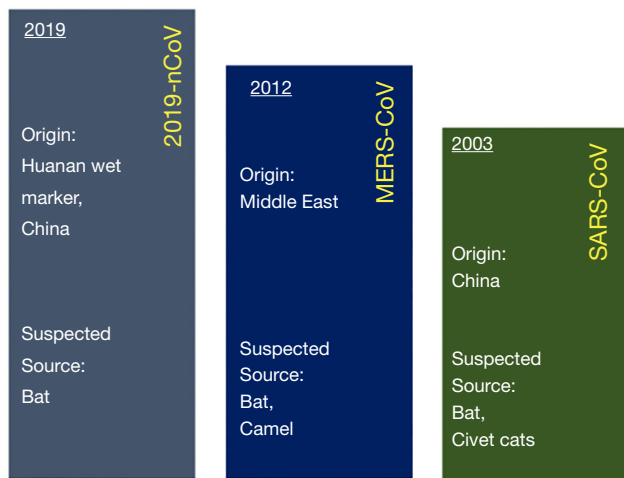
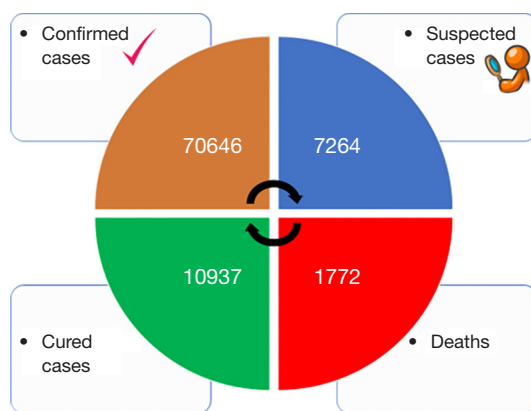


Figure 1 A pictorial description of demographical origin and the suspected source of the all the three coronavirus outbreaks (SARS-CoV, MERS-CoV, and 2019-nCoV infection).



Courtesy: <http://h5.peopleapp.com/covid19/> (updated till 02/18/2020)

Figure 2 Total number of confirmed, suspected, cured and death cases within China (updated till 02/18/2020).

acute respiratory syndrome-related coronavirus (SARS-CoV) epidemic in 2003 and the Middle East respiratory syndrome coronavirus (MERS-CoV) epidemic in 2012 (Figure 1). In December 2019, clusters of acute respiratory illness cases were reported among people associated with the Hunan seafood and animal market in the city of Wuhan, China. Within 1 month of reporting of a novel coronavirus associated acute respiratory illness, more than 70,000 confirmed cases have been confirmed with a reported mortality of around 2% to 3% in these patients (2-4). In China alone, the total number of confirmed COVID-2019

Table 1 Epidemiological data of total confirmed, cured and died cases in China

Area	Confirmed cases	Cure cases	Death
Hubei province	58,182	6,639	1,696
Guangdong province	1,322	473	4
Henan province	1,246	438	16
Zhejiang province	1,171	470	0
Hunan province	1,006	467	3
Anhui province	973	293	6
Jiangxi province	930	275	1
Jiangsu province	626	226	0
Chongqing	552	210	5
Shandong province	541	182	2
Sichuan province	495	136	3
Heilongjiang province	457	80	11
Beijing	381	114	4
Shanghai	332	161	1
Hebei province	301	109	3
Fujian province	290	84	0
Shaanxi province	240	74	0
Guangxi Zhuang Autonomous Region	238	51	2
Yunnan province	171	47	0
Hainan	163	52	4
Guizhou province	146	55	1
Shanxi province	129	50	0
Tianjin	125	46	3
Liaoning province	121	41	1
Gansu province	91	58	2
Jilin province	89	30	1
Xinjiang Uygur Autonomous Region	75	12	1
Inner Mongolia Autonomous Region	72	8	0
Ningxia Hui Autonomous Region	70	33	0
Hong Kong Special Administrative Region	60	2	1
Taiwan province	22	2	1
Qinghai province	18	13	0
Macao Special Administrative Region	10	5	0
Tibet Autonomous Region	1	1	0
Grand total	70,646	10,937	1,772

Courtesy: <http://h5.peopleapp.com/covid19/> (updated till 02/18/2020)

Table 2 Epidemiological data of total confirmed, cured and died cases worldwide

Area	Confirmed cases	Cure cases	Death
Japan	519	1	1
Singapore	75	19	0
Thailand	35	14	0
Korea	30	10	0
Malaysia	22	9	0
Vietnam	16	7	0
Germany	16	1	0
United States	15	3	0
Australia	15	5	0
France	12	4	1
United Arab Emirates	9	4	0
United Kingdom	9	8	0
Canada	8	1	0
Italy	3	0	0
India	3	0	0
Philippines	3	0	1
Russia	2	0	0
Spain	2	0	0
Sri Lanka	1	1	0
Cambodia	1	0	0
Finland	1	1	0
Sweden	1	0	0
Belgium	1	0	0
Nepal	1	0	0
Egypt	1	0	0
Grand total	801	88	3

Courtesy: <http://h5.peopleapp.com/covid19/> (updated till 02/18/2020).

cases reported till 18th January 2020 is 70,646 with another 7,264 suspected to have COVID-2019 and are pending test results (*Figure 2*). Excluding China, around 801 laboratory-confirmed cases have been reported from 25 countries worldwide. The bulk of these cases are reported mostly from Japan, Singapore, Thailand, and Korea. As of 18th February 2020, 15 confirmed cases have been reported in the United States (5). While 1,772 deaths have been

reported among patients suffering from COVID-2019 in China alone, only 3 deaths have been reported worldwide 1 each from Japan, Thailand, and the Philippines (*Tables 1,2*).

Zoonotic component of 2019-nCoV

While we still do not know the exact source of origin of 2019-nCoV, the early cases were speculated to be the result of animal-to-person spread with a possible epidemiological link to the Huanan seafood wholesale market (6). As the subsequent cases were reported even in individuals without any exposure to animal markets, it is now thought that the growing number of cases are secondary to the subsequent person to person contact (*Figure 3*). Metagenomic analysis using next-generation sequencing has shown that this virus has 96.2% homology to a bat virus and shares 79.5% of its genetic sequence with SARS-CoV (6).

Genomics analysis of 2019-nCoV

Coronavirus, an enveloped positive-sense RNA virus has multiple club-like spikes on its surface which give an appearance of Sun's corona during a total solar eclipse. The family Coronaviridae incorporates many viruses predominately found in birds and mammals (*Figure 4*). It was in the 1960s, when a large percentage of respiratory infections in humans were traced to be related to coronaviruses and henceforth it was postulated that, humans could also become accidental hosts in case of contact with wild and exotic animals. 2019-nCoV is being studied for its genetics by researchers and scientists worldwide and the recent report by Paraskevis *et al.* suggests its genomes to be non-mosaic thereby rejecting a hypothesis of a possibility of recent recombination event as the cause of this outbreak (7). Instead, there is a possibility of COVID-2019 to be originating from bat considering its close similarity to bat coronavirus. However, more dedicated studies are needed to understand additional insights about its pathogenesis and origin.

Approach to a suspected case

It is important for the health care professionals to understand the steps which need to be followed in case of suspicion of COVID-2019 in any of their patients. WHO and CDC have issued statements regarding when to suspect? Whom to suspect? And how to approach? Initially, suspected case definition [NCIP (Novel coronavirus infected pneumonia)] was based on the previous

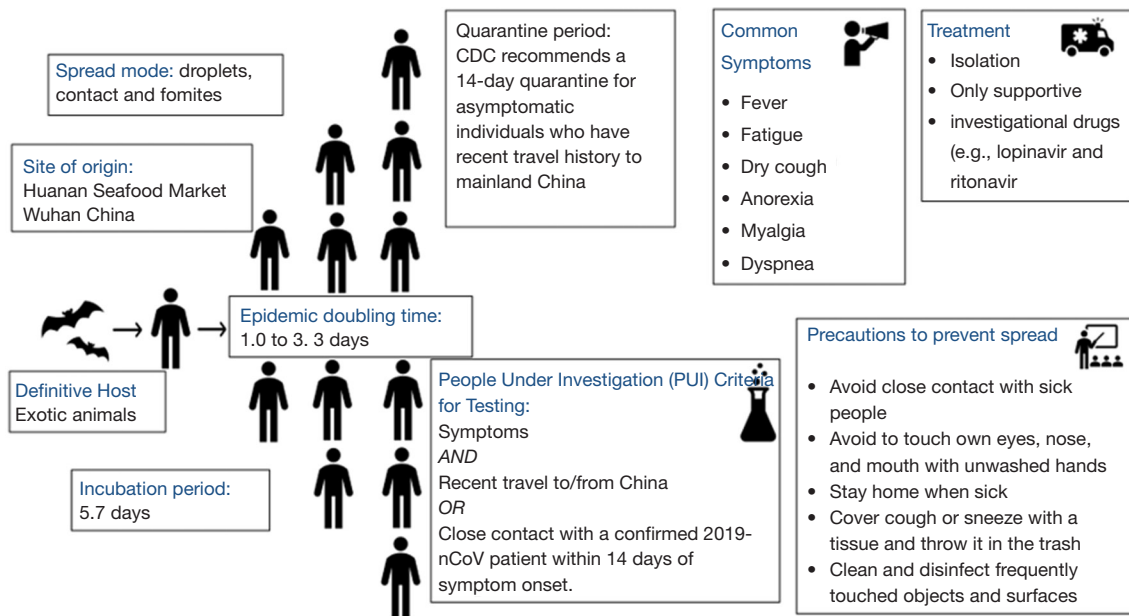


Figure 3 A proposed pictorial description of various phases of dissemination of 2019-nCoV from animals to humans, symptoms, available treatment strategies, and preventive measures.

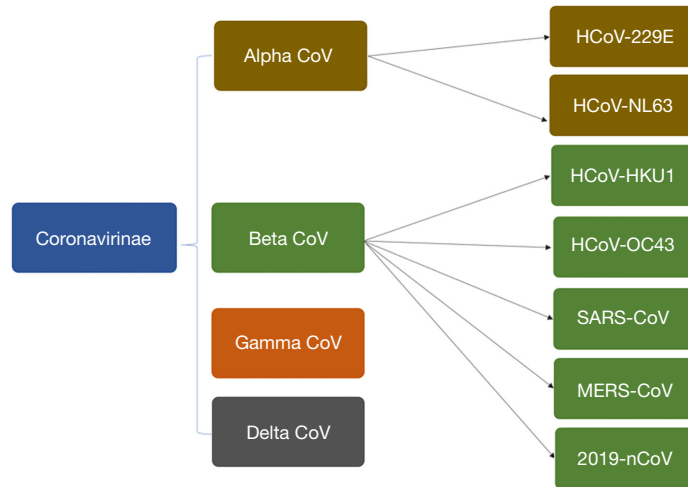


Figure 4 The figure describing Coronavirinae family and subgroups with the new addition of 2019-nCoV in the beta-CoV subgroup.

experiences with MERS and SARS virus outbreaks. Later, on 18th January 2020, WHO modified the definition that categorically removed the laboratory and imaging criteria in order to expedite the diagnosis. Hence, now the new criteria of suspected case is based on clinical and travel history alone, which is helping to investigate and isolate suspected

cases without any further delay (8) (*Table 3*).

It is expected that health care professionals be thorough with the stepwise approach to investigate any case of COVID-2019 as per CDC guidelines (9). Through a flowchart, we simplified the guidelines in a stepwise fashion (*Figure 5*).

Table 3 Criteria laid down by WHO for the suspected case, NCIP, close contact and people under investigation

Terminology	Defining criteria
1. Suspected NCIP case Definitions (based on SARS and MERS case definition)	<ul style="list-style-type: none"> ✓ All following four criteria's (I) Fever (II) Radiographic evidence of pneumonia (III) Low/Normal WBC count or low lymphocyte count (IV) No response to antibiotics despite 3 days of treatment <p>OR</p> <ul style="list-style-type: none"> ✓ Above first three criteria's (1,2, and 3) <p>AND</p> <p>An epidemiological link to Huanan market or contact with patients with similar symptoms</p>
2. Epidemiologic criteria to define a suspected case (updated definition on 01/18/2020)	<p>Fever</p> <p>OR</p> <p>Signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath)</p> <p>AND</p> <p>Any one of the following</p> <ul style="list-style-type: none"> (I) Any person, including health care workers, who has had close contact with a laboratory-confirmed 2019-nCoV patient within 14 days of symptom onset (II) A history of travel from mainland China within 14 days of symptom onset
3. People Under Investigation (PUI) case	Suspected case based on epidemiologic criteria (as mentioned above) for whom the laboratory result for 2019-nCoV is pending
4. Confirmed case	<p>Any case who has a positive test for 2019-nCoV by one or more of following methods</p> <ul style="list-style-type: none"> (I) Isolation of 2019-nCoV (II) At least 2 positive results by real time reverse-transcription-polymerase chain reaction (III) A genetic sequence that matches 2019-nCoV
5. Close contact	<p>A close contact is defined as:</p> <ul style="list-style-type: none"> ✓ Being within approximately 6 feet (2 meters) of a COVID-19 case for a prolonged period <p>OR</p> <ul style="list-style-type: none"> ✓ Having direct contact with infectious secretions of a COVID-19 case

NCIP, novel coronavirus infected pneumonia; COVID-19, Coronavirus disease 2019; SARS, severe acute respiratory syndrome-related coronavirus; MERS, Middle East respiratory syndrome coronavirus; PUI, People Under Investigation.

Clinical features, lab abnormalities and treatment outcome based on available literature

Many observational studies mostly being reported from Mainland China have described the clinical features, treatment given and outcomes of the patients suffering from COVID-2019 induced NCIP. Wang *et al.* from the Hospital of Wuhan University have studied 138 infected and hospitalized patients (10). The median age reported was

56 years and predominantly affecting the males. Common symptoms reported were fever (98.6%), fatigue (69.6%) followed by dry cough (59.4%). With regards to laboratory workup, patients were found to have lymphopenia (70.3%), deranged coagulogram (58%), elevated lactic acid dehydrogenase (39.9%) and abnormal imaging findings (100%). The most common imaging findings were bilateral patchy shadows and ground-glass opacities. Patients were treated with varied treatment regimens including antiviral



Figure 5 A stepwise approach to a suspected case of 2019-nCoV based on CDC guidelines.

agents (oseltamivir), antibacterial agents (moxifloxacin, azithromycin, and ceftriaxone) and steroids. Twenty-six point four percent of patients required intensive care unit (ICU) support with the majority requiring invasive ventilation. The patients of older age group (66 *vs.* 51 years) and with underlying comorbidities (72.2% *vs.* 30.6%) had more likelihood of requiring ICU level care. The most common complications reported were acute respiratory distress syndrome (61.1%), arrhythmia (44.4%), and shock (30.6%). The other complications noted were acute cardiac injury, acute renal injury, pneumothorax, and secondary bacterial infections. Hypertension (31%), followed by cardiovascular disease (14.5%), and diabetes mellitus (10%) were the top co-existing comorbidities. The average duration of hospital stay amongst the individuals who were discharged was 10 days. The overall reported mortality rate was 4.3%.

Another study by Huang *et al.* reported from the central hospital of Wuhan included 41 COVID-2019 patients (11). When compared with Wang *et al.*'s cohort, Huang *et al.*'s patient population were comparatively younger (median age of 49 *vs.* 56 years) and with lower mortality

rate (3% *vs.* 4.3%). Both study groups had the same top 3 clinical features (fever, fatigue, and cough) and underlying comorbidities (hypertension, diabetes mellitus, and cardiovascular disorders). In general, viral infections are known to have the worst outcome for immunocompromised individuals (12-18). The similar results of different studies in terms of clinical presentation, underlying comorbidities and mortality rates would certainly be helpful to health professionals to triage and risk stratify the patient population who might require a high level of care (10,11,19-21). As per the latest available data, the total number of deaths related to COVID-2019 is the highest of all the three coronavirus outbreaks of the 21st century. However, until now, the mortality rate secondary to COVID-2019 is the lowest of all, with the highest being associated with MERS-CoV (35%) followed by SARS-CoV (9.6%) and 2019-nCoV (2.72%) (Figure 6).

Newer drugs and active clinical trials

Since the time of COVID-2019 outbreak, there has been a sudden surge in the number of clinical trials getting

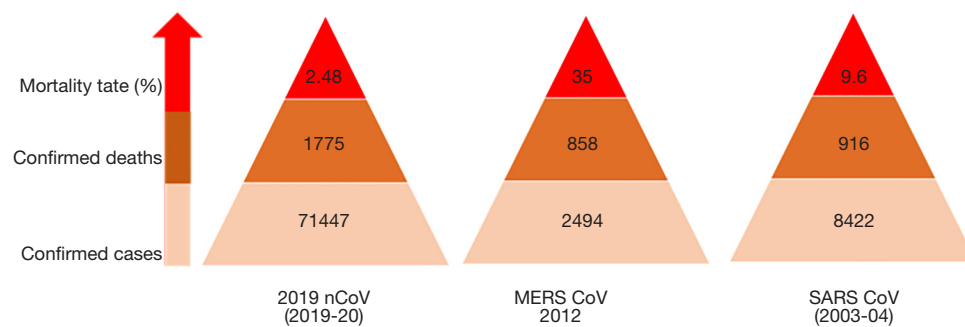


Figure 6 Comparing confirmed cases, total deaths and mortality rates worldwide between three coronavirus outbreaks of 21st Century (2019-nCoV versus MERS CoV versus SARS CoV).

approved for studying various aspects of 2019-nCoV infection, its pathogenesis, symptomatology, complications and newer diagnostic and treatment alternatives (22,23). As per the *clinicaltrials.gov*, we found many clinical trials actively recruiting patients with most of the studies being initiated in Chinese hospitals (Table 4). For example, there are studies looking into the impact of COVID-2019 on the cardiovascular system (Gov Identifier: NCT04255940) or on psychological status of health care professionals (Gov Identifier: NCT04260308). Similarly, there are clinical trials exploring newer treatment options like hydroxyquinoline (Gov Identifier: NCT04261517), methylprednisone (Gov Identifier: NCT04263402), Immunoglobulin (Gov Identifier: NCT04261426), Darunavir/Cobicistat (Gov Identifier: NCT04252274), Lopinavir/Ritonavir (Gov Identifier: NCT04261907) and so on. WHO and the National Health Commission of the People's Republic of China have allotted separate financial aid as well for conducting studies. While we appreciate every attempt that could help in better treatment of the patients affected with this deadly virus, the results of these trials would not be available in near future to be of immediate benefit to the presently affected population. Hence, based on the experiences with previous coronavirus outbreaks, we believe that supportive treatment is the best way to treat a patient and exercising all the precautionary and preventive measures is the only way to avoid ourselves from acquiring infection.

Hospital policies and preparedness

Employee, patient, community safety—hospital's priority

Every hospital, be it a community health center or a university or an academic center is expected to be vigilant, resourceful, and upgraded to tackle any COVID-2019 case

efficiently. Every hospital should have dedicated task force coordinating the hospital's internal processes and resources to promote effective and safe management of any local outbreak of the coronavirus, if the situation arises. Also, it would be desirable for the special task force to work closely with the local health department and the Centers for Disease Control and Prevention (CDC) to prepare and respond to any potential 2019-nCoV cases that may present to the hospital. There should be special seminars and educational sessions for health care workers focusing on CDC guidelines for identification and treatment of patients with suspected or confirmed cases of the coronavirus.

Additional precautions in hospitals

Signage

Posting signage at all entries, in several languages, advising patients or visitors to alert staff immediately regarding recent travel, current symptoms, and/or close contact with someone who fits these criteria.

Screening

Asking all patients the CDC screening questions. Symptoms including fever, cough, or shortness of breath. In addition, travel questions including travel to Hubei Province and/or mainland China. Finally, also asking about close contact with a confirmed coronavirus patient, or someone who has traveled from mainland China with symptoms requiring hospitalization, within the last two weeks.

Personal protective supplies

To ensure that the hospital provides adequate supplies of personal protective equipments, such as gowns, gloves, masks, face shields, and goggles to its staff and physicians.

Table 4 Recent clinical trials actively recruiting/studying various aspects of 2019-nCoV characteristics, newer diagnostics and treatment options

Clinical trials.gov identifier	Status	Study type	Expectant participants	Study title	Country
NCT04262921	Active & Recruiting	Observational	500	Clinical Characterisation Protocol for Severe Emerging Infections (CCP-nCoV)	France
NCT04244591	Active & Recruiting	Interventional	80	Glucocorticoid Therapy for Novel Coronavirus Critically Ill Patients with Severe Acute Respiratory Failure (Steroids-SARI)	China
NCT04251871	Active & Recruiting	Interventional	150	Treatment and Prevention of Traditional Chinese Medicines (TCMs) on 2019-nCoV Infection	China
NCT04261517	Active, not yet recruiting	Interventional	30	Efficacy and Safety of Hydroxychloroquine for Treatment of Pneumonia Caused by 2019-nCoV (HC-nCoV)	China
NCT04259892	Active & Recruiting	Observational	300	Viral Excretion in Contact Subjects at High/Moderate Risk of Coronavirus 2019-nCoV Infection (Cov-CONTACT)	France
NCT04252274	Active, not yet recruiting	Interventional	30	Efficacy and Safety of Darunavir and Cobicistat for Treatment of Pneumonia Caused by 2019-nCoV (DACO-nCoV)	China
NCT04245631	Active & Recruiting	Observational	50	Development of a Simple, Fast and Portable Recombinase Aided Amplification Assay for 2019-nCoV	China
NCT04255940	Active & Recruiting	Observational	12,000	2019-nCoV Outbreak and Cardiovascular Diseases	China
NCT04256395	Active & Recruiting	Observational	100,000	Efficacy of a Self-test and Self-alert Mobile Applet in Detecting Susceptible Infection of 2019-nCoV (2019-nCoV)	China
NCT04264533	Active, not yet recruiting	Interventional	140	Vitamin C Infusion for the Treatment of Severe 2019-nCoV Infected Pneumonia	China
NCT04261907	Active, not yet recruiting	Interventional	160	Evaluating and Comparing the Safety and Efficiency of ASC09/Ritonavir and Lopinavir/Ritonavir for Novel Coronavirus Infection	China
NCT04257656	Active & Recruiting	Interventional	452	A Phase 3 Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Remdesivir in Hospitalized Adult Patients with Severe 2019-nCoV Respiratory Disease	China
NCT04269525	Active & Recruiting	Interventional	10	Umbilical Cord (UC)-Derived Mesenchymal Stem Cells (MSCs) Treatment for the 2019-novel Coronavirus (nCoV) Pneumonia	China
NCT04260308	Active & Recruiting	Observational	30,000	A Survey of Psychological Status of Medical Workers and Residents in the Context of 2019 Novel Coronavirus Pneumonia	China
NCT04260594	Active, not yet recruiting	Interventional	380	Clinical Study of Arbidol Hydrochloride Tablets in the Treatment of Pneumonia Caused by Novel Coronavirus	China
NCT04264858	Active, not yet recruiting	Interventional	10	Treatment of Acute Severe 2019-nCoV Pneumonia with Immunoglobulin from Cured Patients	China
NCT04263402	Active, not yet recruiting	Interventional	100	The Efficacy of Different Hormone Doses in 2019-nCoV Severe Pneumonia	China
NCT04261270	Active, not yet recruiting	Interventional	60	A Randomized, Open, Controlled Clinical Study to Evaluate the Efficacy of ASC09F and Ritonavir for 2019-nCoV Pneumonia	China
NCT04254874	Active, not yet recruiting	Interventional	100	A Prospective, Randomized Controlled Clinical Study of Interferon Atomization in the 2019-nCoV Pneumonia	China

Table 4 (continued)

Table 4 (continued)

Clinical trials.gov identifier	Status	Study type	Expectant participants	Study title	Country
NCT04255017	Active, not yet recruiting	Interventional	400	An Open, Prospective, Randomized Controlled Cohort Study to Compare the Efficacy of Three Antiviral Drugs (Abidol Hydrochloride, Oseltamivir and Lopinavir/Ritonavir) in the Treatment of 2019-nCoV Pneumonia	China
NCT04261426	Active, not yet recruiting	Interventional	80	The Efficacy of Intravenous Immunoglobulin Therapy for Severe 2019-nCoV Infected Pneumonia	China
NCT04252664	Active, not yet recruiting	Interventional	308	A Phase 3 Randomized, Double-blind, Placebo-controlled Multicenter Study to Evaluate the Efficacy and Safety of Remdesivir in Hospitalized Adult Patients with Mild and Moderate 2019-nCoV Respiratory Disease	China
NCT04268537	Active, not yet recruiting	Interventional	120	Immunoregulatory Therapy for 2019-nCoV-induced Severe Pneumonia Patients	China
NCT04251767	Enrolling by invitation	Interventional	40	To assess Washed Microbiota Transplantation for Patients With 2019-nCoV Infection	China
NCT04252118	Active & Recruiting	Interventional	40	To assess Safety and Efficiency of Mesenchymal Stem Cell in Treating Pneumonia Patients Infected With 2019 Novel Coronavirus	China

Adopted from: <https://clinicaltrials.gov/ct2/results?cond=coronavirus>.

Employee guidance

As an employee, if someone reports having (I) a history of travel from Hubei Province, China, and/or, (II) a history of travel to mainland China requiring subsequent hospitalization, he/she cannot work for 14 days. Similarly, if an employee had close contact with a confirmed case of 2019-nCoV, he/she cannot return to work within 14 days of the last contact. Also, if an employee meets the criteria as described above, he/she should provide a letter from his/her healthcare provider allowing to return to work. However, if an employee has exposure to a confirmed case of 2019-nCoV as a healthcare provider with the use of Personal Protected Equipment in accordance with policy, the above-mentioned criteria should not apply.

The need of the hour: a multi-level collaboration

The 2019-nCoV infection has deeply affected every individual, society, and Nationals all around the world. In the era of free communication, we would like to emphasize the importance of recognizing our responsibilities and fulfilling the expectations of an ideal national (Figure 7). Similarly, we expect and encourage various social media platforms and news channels responsible for broadcasting the latest updates on 2019-nCoV infection and other related subjects to abide

by the regulations and try to maintain transparency while reporting. Recently, WHO has even labeled the rumors and fake news floating in various social media platforms as “Infodemic”. WHO has even initiated a web page “myth busters” to bust rumors and prevent unnecessary panic (24). WHO has sent an expert team to China and is working in close collaboration with Chinese counterparts in order to try to contain the virus and to study the characteristics of the 2019-nCoV, the reason for the outbreak, source of infection and modes of prevention and treatment.

Health care workers: endangering own’s life for community service

As per the reports from China’s National Health Commission, till 16th February a total of 1,716 medical health workers from China alone have been found to be positive for 2019-nCoV, and out of them, 6 health care workers have even lost their life. Most of the health professionals belong to Hubei Providence which is considered as the center of the outbreak. Dr. Li Wenliang, a young 33-year-old ophthalmologist was the whistleblower of the “SARS-like” virus in early December 2019 when the cluster of patients were admitted for pneumonia of unknown etiology. Unfortunately, he died from the



Figure 7 Pictorial descriptions of expected responsibilities of individuals, media houses and international health organizations in containing the spread of 2019-nCoV infection and rumors.

COVID-2019 on February 7, 2020. We would like to pay our regards and homage to all the health care providers including doctors, nurses, staff members, researchers, scientists, and all other officials who in one or the other way are involved in providing their services to the COVID-2019 struck community.

Conclusions

In conclusion, as of now, we have very little knowledge about 2019-nCoV, and every attempt should be made in order to understand and contain COVID-2019 as early as possible. We hope that the ongoing clinical trials will help us to gain further insights about its genetics, source of origin, pathogenesis, diagnosis, and treatment.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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