

Emergence of COVID-19 Infection: What Is Known and What Is to Be Expected – Narrative Review Article

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Keywords

Coronavirus outbreak · COVID-19 · Emerging epidemics · Emerging infections · Novel coronavirus

Abstract

Background: The discovery of the coronavirus disease 2019 (COVID-19) during a pneumonia outbreak in Wuhan city (China) has raised a global public health concern, as the city consists of around 11 million people and is considered a major transport and logistics hub. This deadly virus caused the world to be in high alert as the death toll and the number of confirmed cases is continuously rising since the first case was reported. The Chinese government warned that the transmission ability of the virus is increasing, and international efforts are needed to overcome this outbreak. The purpose of this review is to focus on the published articles about the new virus, which will give an insight into the current state of research and data available, as well as recommending future studies. **Methods:** For this narrative review, more than 20 relevant scientific articles and reports were considered from various databases (e.g., Google Scholar, PubMed and Science Direct) using keywords such as Coronavirus Outbreak, COVID-19, Emerging Epidemics, Emerging Infections, and

Novel Coronavirus. **Results:** The results from this review show that the situation is rapidly evolving, as human-to-human transmission is occurring, and the number of new cases and mortalities is increasing by the day and on a global level. There is still ambiguity about mutation risks and how the virus spreads as the source was not yet identified. Major gaps in knowledge about the origin of the virus, epidemiology and transmission impose a great challenge, which emphasizes the need for further studies in the future.

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Introduction

Coronaviruses are a large family of viruses that can cause a range of illnesses from common cold all the way up to more severe diseases such as the Middle East Respiratory Syndrome (MERS) and the Severe Acute Respiratory Syndrome (SARS), which are known to cause severe respiratory and intestinal illnesses. Most of the coronaviruses live in animals; however, the SARS outbreak in China between 2002 and 2003 had changed this fact when a coronavirus jumped from an animal reservoir and infect-

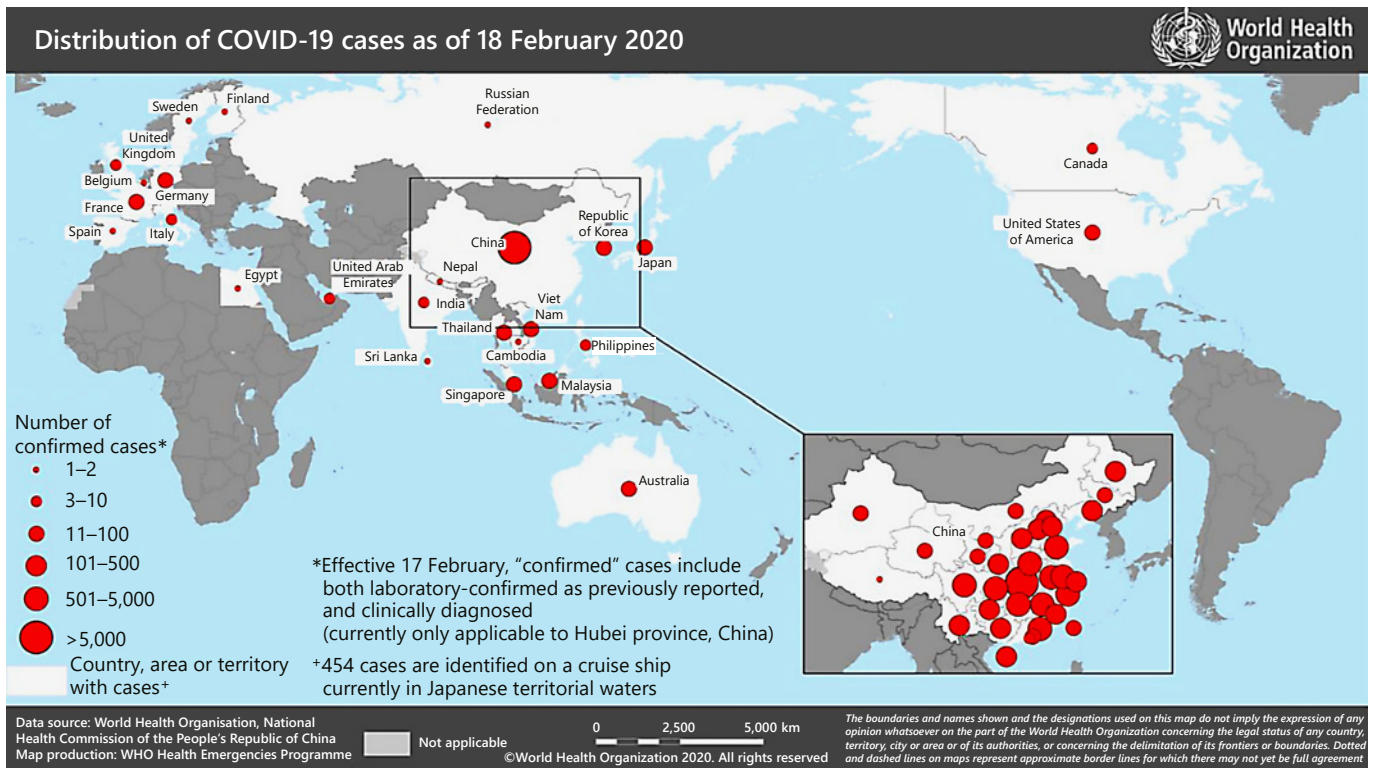


Fig. 1. Countries, territories or areas with reported confirmed cases of COVID-19, February 18, 2020.

ed individuals from China at first, and then “exploded into a global pandemic of about 8,000 cases and 774 deaths over a period of several months” [1].

According to the Center for Disease and Control Prevention, “229E, NL63, OC43, and HKU1 are the most common human coronaviruses out of the seven viruses identified” [2]. COVID-19, first identified in China, is a new strain of coronaviruses that has not been previously identified in humans but was linked to animal sources. The virus is believed to be transmitted from animals to humans at first, and then from humans to humans through airborne droplets of infected patients’ fluids, which has led the virus to infect and kill thousands of people and to raise international concern.

The global distribution of COVID-19 is expanding day by day (Fig. 1) as per the World Health Organization situation report [3]. According to the data updated on February 18, 2020, the total number of confirmed cases has reached 72,528 with 1,870 deaths from China only.

The WHO risk assessment for acute public health events and disease transmission classified the risk of COVID-19 transmission as very high, high and high in China, at a regional level, and at a global level, respectively [3]. The European Center for Disease Prevention and

Control has also reported high COVID-19 transmission and potential outbreak impacts.

The incubation period is estimated to be between 2 and 15 days, and transmission from asymptomatic cases has been reported [4]. More COVID-19 cases are expected in the upcoming days due to the increase in screening and detection methods, and the biggest threat to be considered here is the mobility of these infected individuals.

Clinical and Epidemiological Characteristics

In order to understand the disease characteristics and outcomes, Huang et al. [5] collected and analyzed data from 41 COVID-19 confirmed patients. According to them, many of the early cases identified were linked to the Huanan seafood and animal market in Wuhan as 27 of the patients reported market exposure, which suggests that a likely source of the new virus might have been an animal.

A Centers for Disease Control and Prevention report explained that “there is still unclear clinical picture about COVID-19 as some of the infected patients will show no or mild symptoms such as shortness of breath, cough and

fever, while others will start developing more serious complications like pneumonia and kidney failure” [6]. Huang et al. [5] also pointed out the similarities between the clinical presentation of COVID-19 and SARS as both diseases caused clusters of fatal pneumonia: “Although the whole spectrum and pathophysiology of the new disease is still unknown, the current evidence suggests that there is a high likelihood for patients to have intensive care unit admission or end up dying.”

Li et al. [7] addressed the epidemiological characteristics of COVID-19 cases by collecting and analyzing data from the first 425 laboratory-confirmed cases in Wuhan. The results showed that “most of the infected cases were elderly, males and with reported exposure to Huanan seafood market or to another person with respiratory symptoms. In addition, most of those who died from the virus had underlying medical conditions such as cardiovascular diseases or diabetes” [7]. The study’s findings provide an overall useful look at the characteristics of COVID-19 patients; however, they cannot eliminate the fact that some reported cases were females, young individuals and with no previous contact or exposure, which should also be addressed and considered in future studies.

Case Identifications and Virus Transmissibility

Once a suspected case is identified, whether it is symptomatic or asymptomatic, immediate isolation and multiple tests are required to detect COVID-19. The WHO recommends clinical assessment for the signs and symptoms, laboratory testing, nasopharyngeal and oropharyngeal swabs and radiological examination to confirm the results and other associated complications [8]. Many researchers who traced confirmed cases reported the use of real-time reverse-transcriptase polymerase chain reaction test, serological testing, and metagenomics sequencing analysis [9–11].

Transmission dynamics for COVID-19 were assessed in different studies. The initial assessment indicates that the source of this third zoonotic human coronavirus was the seafood and animal market in Wuhan city (China), as they were selling live animals, specifically bats, where the virus was living and then crossed into a human being [7–13]. Although the studies confirmed the relationship between the animal market exposure and the infection, Li et al. [7] pointed out the importance of considering human-to-human transmission as positive cases were confirmed from other geographical areas who have not been exposed to the seafood market.

The investigation of human-to-human transmission started later as transmission cases were reported from individuals within the same family members, and from healthcare workers who were in direct contact with suspected or confirmed cases. An article by Phan et al. [14] explains the possible human-to-human virus transmission as one family cluster of COVID-19 was being reported. The 65-year-old man with underlying health conditions had flown with his wife from Wuhan to Hanoi after the outbreak. The man became ill with fever and fatigue 4 days after traveling and was tested positive for COVID-19 after hospital admission. His son who lives in another city and with no history of traveling to these regions was found to be positive as well, and the investigation showed that he met his parents after they had traveled and stayed with them for 3 days. This article explains the time frame of events very precisely and the possible transmission of the virus from the father to the son after the contact. Although the son has got the infection, the man’s wife and the 28 individuals contacted by the family during their travels were found to be healthy and tested negative to the virus, which requires further explanations and studies to investigate the possible risk factors and the modes of transmission. Furthermore, sequencing of strains from the father and son is needed to confirm the transmission between the two.

Another study by Chan et al. [15] gave information about the risk of infection from close personal contact and estimated the disease incubation period by tracing the travel history of 5 family members who made a visit to Wuhan city from December 29th until January 4th. The study’s clinical, epidemiological, laboratory and radiological findings confirmed COVID-19 infection in the 5 members, in addition to the sixth member who did not visit the city but was found to be infected as well, suggesting a human-to-human transmission.

The basic reproduction number (R_0) for the disease transmission was calculated. According to the European Center for Disease Prevention and Control [6] and Li et al. [7], R_0 for COVID-19 is estimated to be 2.2 (95% CI 1.4–3.9), which is more than 1, indicating infection transmission to the population and estimating that each COVID-19 patient is transmitting the virus to 2.2 individuals. Another study by Tang et al. [4] estimated the basic reproduction number using multiple methods and “reported large-scale outbreak with R_0 equal to 6.47 (95% CI 5.71–7.23) indicating higher transmission of COVID-19.” This high reproduction number supports the beliefs of disease transmission between 3 and 4 generations. As for the modes of transmission, the Centers for Disease Con-

trol and Prevention explain that COVID-19 can spread by close contact from an infected person to another through respiratory droplets during coughing or sneezing. Transmission by touching contaminated surfaces or objects, and then touching the eyes or nose is still unclear and requires the collection of further data [16].

Emerging Coronavirus as a Public Health Emergency

The director-general of the World Health Organization, Doctor Tedros Ghebreyesus, announced on January 23rd that “the emerging COVID-19 is an emergency in China only and not considered as Public Health Emergency of International Concern (PHEIC)” [17]. Until that date, what was known about the disease is that it causes severe respiratory illness symptoms, and that more than 500 cases have been confirmed in China and other countries like South Korea, Japan, the USA, and Thailand.

Due to the previous experience in facing the SARS pandemic, the Chinese government did a great job by meeting the international standards in terms of the isolation of suspected cases, diagnosis and treatment and educational campaigns. But despite this fact, the virus continued to spread due to the mobility of infected cases, and *Lancet* explained that there were concerns due to the daily increase in the number of cases and the many gaps faced as a result of the incomplete and rapidly changing epidemic [17].

Gralinski and Menachery [12] illustrated the emergence and outbreak of COVID-19 in their study showing the timeline for the key COVID-19 events from December 31st, when the cluster of pneumonia cases was reported, until January 23rd. These events include isolating the virus, releasing the genomes, reporting positive cases among travelers from Wuhan, as well as reporting the new cases and deaths in China and globally.

On Thursday, January 30th, the World Health Organization declared COVID-19 as a global public health emergency of international concern, which indicates the international spread of the disease requiring a coordinated global response [18].

Outbreak Containment Measures

The local government in Wuhan has made many attempts to contain the virus. Firstly, they imposed a nationwide ban on wildlife trade in markets, restaurants and e-commerce platforms. Secondly, they closed the seafood

and animal Market in Wuhan in order to collect environmental specimens and to perform environmental sanitation and disinfection. In addition, China’s National Health Commission announced on January 23rd “the suspension of public transportation, with closure of airports, railway stations and highways in the city” to prevent further disease transmission [19].

After cases have been reported from the European Union and European Economic Area (EU/EEA) countries, and due to the high level of movement between China and these countries, the European Center for Disease Prevention and Control emphasized the importance to have an entry and exit screening for travelers, including symptoms and thermal screenings as a method to detect and isolate positive cases [20]. Even though this method can reduce the global spread to other countries, it might not be very efficient, as some infected patients are not showing any symptoms, and others are having symptoms similar to those of the coronavirus, but are actually caused by the common influenza virus.

The Centers for Disease Control and Prevention have responded to the outbreak by “establishing a COVID-19 Incident Management System, activating its Emergency Operations Center to provide ongoing support and responses, issuing updated travel guidance for China to prevent nonessential trips to China, publishing guidance for healthcare workers on the clinical care of COVID-19 patients, and posting a guidance for appropriate assessment and management of patients exposed to COVID-19” [21].

In order to prevent infection to the population and healthcare workers, the Centers for Disease Control and Prevention encourage following simple everyday preventive actions such as to avoid close contact with sick people, to avoid touching the eyes, nose, and mouth with unwashed hands, to wear a face mask and to frequently wash the hands with soap and water or with alcohol-based hand sanitizers [22]. Health promotion campaigns are encouraged in China and globally as part of educating the people to reduce the risk of infection transmission. By educating the people, it is less likely they will get the infection, thus reducing the risk of transmitting the disease to others.

Treatment, Recovery and Vaccination

Up to date, there is no vaccine to prevent COVID-19 and the work on treatment is ongoing [22, 23]. After the person gets infected, the treatment and recovery will be dependent upon the severity of the symptoms and associated complications.

By comparing the number of deaths to the total number of cases, we can see that most of the infected cases are recovering, which is quite promising. China is performing an ongoing clinical trial in order to find a treatment for COVID-19. One of the anti-viral drugs being tested is chloroquine, which has a promising profile against COVID-19 as “patients treated with this drug demonstrated a better drop in fever, improvement of lung CT images, and required a shorter time to recover compared to parallel groups” [24].

Another anti-viral drug investigated by Gilead Sciences is remdesivir. The drug is believed to have potential activity against COVID-19 as “it has demonstrated in vitro and in vivo activity in animal models against MERS and SARS coronaviruses.” Gilead initiated two clinical trials on positive COVID-19 patients with mild and severe clinical manifestations separately. Patient enrolment started in February and it is anticipated for the results to be received in April [25].

The third and last anti-viral drug tested in a 70-patient clinical trial in Shenzhen, Guangdong province, is favilavir, which demonstrated efficacy in treating COVID-19, and with minor side effects. This drug was the first to get the approval to treat COVID-19 from the National Medical Products Administration of China [26].

The work on vaccination is ongoing and many researches and vaccine development plans have been announced from pharmaceutical companies and agencies [27]. Ramaiah and Arumugaswami [28] reported a “detailed analysis of COVID-19 genome evolution and potential universal epitopes for subunit vaccine development.” The study recommended continuous surveillance of coronavirus strains in live animal markets in order to have a better understanding of the viral adaptation to the human host, and to develop practical solutions to prevent the emergence of more novel pathogenic coronavirus strains.

Conclusion and Recommendations

Human-to-human transmission is occurring, meaning that more COVID-19 cases are expected to be reported in the future, which can potentially cause disruptions of global public health systems and economic losses [29]. Although sustained human-to-human transmission is expected in China, this transmission cannot be quantified with the current epidemiological data available. Prevention measures are implemented globally, and investigations are ongoing to find the source of the disease and to

understand more about the virus’s characteristics, illness severity, and transmission routes. Major gaps are presented as the majority of what we know about the virus is based on similar coronaviruses, but the work on treatment is promising. In order to have a better understanding of the new virus, countries should work on providing reliable data through openness and data sharing, as well as conducting further researches on the reported cases. In addition, countries should keep working on improving the preventive measures implemented to reduce the number of infected patients and transmissions at the same time.

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Statement of Ethics

The author has no ethical conflicts to disclose.

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Author Contributions

The author worked on this review during her personal time and with high commitment. This review contributes to the current work available as it gives a clear picture of the current situations, summarizes the key points from each article and gives a recommendation to be fulfilled by future studies.

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