The first cases of COVID-19 in 10 countries: How were they infected?

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Abstract
Recently, a new respiratory infectious disease called COVID-19 has emerged and created a global emergency. It was initially linked to the animal-to-human transmission. However, it is now thought that COVID-19 is spreading through human-to-human transmission mainly via droplets. As there is no definite antiviral therapy for the treatment of cases with COVID-19 the best option for slowing down the pandemic and reducing mortality rates is protecting us against the virus. To achieve this goal obtaining information about how first cases infected with COVID-19 is crucial. Hence, this study aims to review the studies published in peer-reviewed journals to report the first confirmed cases with COVID-19. Herein, we review the origin, symptoms, diagnostic tests, and progress of the disease and possible actions of authorities which would be effective in similar pandemics in the future. This study reviewed 13 cases (5 females and 8 males; 25-61 years old) from 10 countries. All cases have recovered from COVID-19. The results of this review suggested that timely reports of the confirmed cases, notifying World Health Organization and providing information to the general population about the methods of spreading the virus would have decreased the number of infected cases and mortality rates. In addition, the travel history of the first confirmed cases in various countries suggested that prompt actions in restricting travels and closing borders could be an efficient strategy in preventing the transmission of the disease outside of the affected sites. Efforts should be taken by health authorities for preparing the world for future epidemic/pandemic in terms of developing advanced screening strategies in the borders and diagnostic strategies for early identification of infected cases.

Keywords: First cases, COVID-19, 2019-nCoV, Infection, Coronavirus
How the first cases of COVID-19 in 10 countries become infected? a case series

Abstract

Recently, a new respiratory infectious disease called COVID-19 has emerged and created a global emergency. It was initially linked to the animal-to-human transmission. However, it is now thought that COVID-19 is spreading through human-to-human transmission mainly via droplets. As there is no definite antiviral therapy for the treatment of cases with COVID-19 the best option for slowing down the pandemic and reducing mortality rates is protection against the virus of interest. To achieve this goal obtaining information about how first cases infected with COVID-19 is crucial. Hence, this study aims to review the studies published in peer-reviewed journals to report the first confirmed cases with COVID-19. Herein, we review the origin, symptoms, diagnostic tests, and progress of the disease and possible actions of authorities which would be effective in similar pandemics in the future. This study reviewed 13 cases (5 females and 8 males; 25-61 years old) from 10 countries. All cases have recovered from COVID-19. The results of this review suggested that timely reports of the confirmed cases, notifying World Health Organization and providing information to the general population about the methods of spreading the virus would have decreased the number of infected cases and mortality rates. In addition, the travel history of the first confirmed cases in various countries suggested that prompt actions in restricting travels and closing borders could be an efficient strategy in preventing the transmission of the disease outside of the affected sites. Efforts should be taken by health authorities for preparing the world for future epidemic/pandemic in terms of developing advanced screening strategies in the borders and diagnostic strategies for early identification of infected cases.

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Introduction

Several patients with a primary diagnosis of pneumonia appeared in the central province of Hubei in China with unknown causes in December 2019. The newly emerged infectious disease was officially called later COVID-19 leading to an epidemic in China (1, 2). COVID-19 epidemic has rapidly crossed the borders through human to human transmission and disrupted public health systems, global economics and subsequently touched every sector and quality of lives of people across the world, developing a pandemic as declared by the World Health Organization on 11 March 2020 (3).

The underlying cause of COVID-19 has not been fully understood. It is thought that the original cause of COVID-19 was linked to bats similar to the previous SARS-Cov and MERS-Cov epidemics. It has also been suggested that snakes can act as intermediate hosts to transfer COVID-19 from bats to humans (1). Given the high incidence and prevalence of the disease, growing human-animal interface, genetic diversity and recombination events across the genomes (3), the outbreak of COVID-19 is likely undertaken by super shaping phenomenon as previously suggested as the main cause for spreading SARS-CoV and MERS-CoV (4). COVID-19 is
considered as a multi-organ failure disease in which can involve kidney, respiratory system and other organs (5-7).

As of Tuesday 24 May 2020, The US has the highest number of infected cases (1547973) followed by Brazil (310087), UK (254199), Spain (234824), Italy (228658) and Germany (177850). The US has the highest number of death (92923) followed by Kingdom (36390), Spain (28628), Brazil (20047), Italy (15632) and Germany (8216). While the exact underlying mechanism for spreading the virus is still not clearly understood, it is known that the countries with proximity to China and strong travel and migration history with China have had a higher number of cases infected with the COVID-19. Looking at the first COVID-19, we see a link between direct or indirect travel history to China.

Given a large number of infected people and mortality rates caused by the COVID-19 crisis, many countries have adopted restrictive measures to minimize the number of cases and death, yet the numbers are still increasing in some countries. The increasing number of cases and death along with the strict restrictive measures together affects people's mental health and well-being. Therefore, it is critical to identify possible modes of transmission to be equipped with efficient precaution recommendations and infection prevention guidelines to minimize infection transmission and related consequences on the quality of lives of people in future similar situations. Hence, the present paper reviews all peer-reviewed studies that reported the first cases of COVID-19 disease diagnosed in 11 countries between 05 January 2020 and 09 February 2020. Such an analysis provides a better understanding of the spreading mechanism of the virus and provides information for preparedness, early identification of cases and secondary prevention in future potential epidemics or pandemics, and contributes to improvement in the quality of lives of people across the world. The cases were divided into two categories of cases with and without travel history to Wuhan.

**Reported cases with travel history**

**Cases with travel history to Wuhan, China**

COVID-19 disease was confirmed for the first time in Yan’an in China. A 60-year-old man from Yan’an, China with a history of travel to Wuhan was the first case in the world who spread the COVID-19 virus. The patient visited the emergency department with a chief complaint of 5-day fatigue without any respiratory symptoms. On identifying his 5-day unexplained fatigue a patchy high-density shadow in both lungs was found in his chest CT scan with a negative result for the oropharyngeal swab for COVID-19 on the real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) assay. Laboratory tests revealed a slight decrease in lymphocyte count and an increase in blood levels for erythrocyte sedimentation rate, C-reactive protein, and high-sensitivity C-reactive protein. The white blood cell count and D-dimer were normal. He was admitted to the department of respiratory and critical care medicine and received treatment. Five days after receiving treatments a chest CT scan showed that the dorsal part of the right upper lobe and lower lobe of both lungs developed patchy consolidation with a ground-glass-like
shadow around them and grid shadows along with bronchial inflation. The second oropharyngeal swab for 2019-nCoV nucleic acid test was positive 6 days after the onset of the symptoms when the diagnosis of 2019-nCoV pneumonia was confirmed. The patient did not develop any other clinical symptoms during hospitalization. Details of treatment and duration of the hospitalization were not reported by the authors (4).

Nepal was one of the countries bordered with China that reported its first case of 2019-nCoV. The first infected patient with COVID-19 virus in Nepal was a 32-year man who was a university student in Wuhan, without any underlying conditions and no history of exposure to Wuhan wet market. In his return to Nepal only 10 days after he originally felt sick in China, he was visited at an outpatient department of a tropical and infectious disease hospital with a chief complaint of cough. The patient’s throat swabs were tested positive for COVID-19 on real time RT-PCR and the upper lobe of his left lung showed an infiltrate in the chest radiogram. The patient was admitted to the hospital and isolated with 37.2°C temperature and throat congestion and without any other relevant signs or symptoms. Six hours after a protocol of broad-spectrum antibiotics and supportive therapies were provided for him, he had mild difficulties with breathing and decreased oxygen saturation. On the second day of his admission, he presented 38.9°C fever followed by more severe breathing difficulties in the supine position along with crepitations in the lower part of the right lung. On the third day of his admission, he did not show fever and his clinical symptoms were improved. His lab tests returned normal and he was discharged from the hospital the next day with a self-quarantine instruction at home. All laboratory tests for influenza virus type A and B, dengue viruses, Brucella and scrub typhus were negative at the discharge. His real-time RT-PCR throat swab was negative for COVID-19 on two follow up assessments. The patient was categorised as a mild COVID-19 and was recovered in 4 days (8).

In Taiwan, the first case had different clinical features and developed typical symptoms related to COVID-19. A 55-year-old woman who worked in Wuhan, China without any underlying condition and exposure to Huanan Seafood Wholesale Market and sick people developed a sore throat, dry cough, fatigue, and low-grade subjective fever. The symptoms were released after she used over-counter medication. After 9 days she returned to Taiwan and immediately presented to quarantine due to the history of developing symptoms. She had low-grade fever of 38.0°C and 88-90% oxygen saturation under ambient air in the quarantine. The next day the real-time RT-PCR throat swab resulted in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and she was admitted to hospital while she had stable vital signs except for the sore throat, intermittent dry cough and exertional dyspnea. The supplement oxygen therapy was administered by nasal cannula (3Litre/minute). The lab investigation showed lymphopenia and elevated C-reactive protein, alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase. The results of a chest X-ray showed bilateral perihilar infiltration and ill-defined patchy opacities. On the first days of hospitalization, the patient received antitussive agent, saline
infusion and empiric antibiotic with ceftriaxone (2 gm everyday intravenously and 2 gm loading) followed by oral amoxicillin/clavulanate 875/125 mg every 12 h on the 8th day of admission to hospital. One week later her real-time RT-PCR of sputum specimens yielded negative results and remained negative 6 days later and serial X-ray and chest CT scan revealed tenacious COVID-19 pneumonia and sequelae. The patient discharged on the 28th day of the illness after 17 days of hospitalization when the results of the tests returned negative for SARS-CoV-2 (9).

Another case was a 25-year-old Vietnamese woman who traveled to Wuhan and stayed there for 2 months with two Vietnamese friends. They confirmed that they did not have any exposure to the wet market and contact with sick people. They all returned to Vietnam together on the same date and flight. On the 6th day after they returned to Vietnam, the patient displayed fever, fatigue, coughing, sneezing, and mild chest pain. She visited a local hospital where she was suspected of severe COVID-19 and referred to a relevant hospital. Her two colleagues also displayed similar symptoms and were admitted to a different hospital and tested positive for COVID-19. A nasopharyngeal swab specimen revealed negative results for all relevant pathogens and her nasopharyngeal specimen test was positive for SARS-CoV-2 after 6 days. The clinical symptoms including high fever, chest pain and dry cough remained for 2 days and were managed on day 3 of her admission to hospital followed by an improvement in cough and chest pain on day 5. The patient discharged on day 9 (10).

The case report published to report the first cases in South Korea employed a different approach in the report and highlighted three cases among the first 24 cases. The first South Korean patient was a 35 years old woman who developed pneumonia in three days after onset of her symptoms with no pneumonia clinical features, and with a travel history to Wuhan. The reason behind the early identification of pneumonia was only scanning her lungs with a high-resolution computed tomography scan. The patient developed severe clinical symptoms with high oxygen demand for more than two weeks. The second highlighted patient contracted the infection in Japan and transferred it to the third case who spread the virus to three family members. The other first cases were infected through family/friend transmission, conference attendance, travel history to Wuhan, Singapore, Thailand and Japan or contact with diagnosed cases (11).

In sum, in these Asian countries bordered with China, the transmission of the virus has been predictable due to their proximity to China and the fact that these countries have a large number of populations with Chinese ethnicity who had traveled to China during Chinese New Year Holiday. However, the rapid spread of the virus within two weeks beyond the borders of Asian countries suggest that the COVID-19 is able to spread rapidly from its original source to other countries through human to human transmission regardless of the geographic distance. France, Italy, the United States and Canada are four countries where reported their first cases who originated from travel to Wuhan. France was one of the European countries where reported the first three cases who had history of residence in or travel to China without any exposure to wet market, sick people and live animals during their residence in or travel to China 14 days before the onset of their symptoms.
The first case in France was a 48-year-old man who traveled to different cities in China including Wuhan. On the second day of his arrival to China, he visited his family members and friends. He showed the initial symptoms including fever, headache, and cough 6 days before he returned to France. He returned to France via three airports. The next day he visited a GP and was suspected to either severe acute lower respiratory infection or an acute respiratory illness. The patient was transferred to and isolated in a hospital. On the next day, the results of his rt-PRC test for SARS-CoV-2 was positive. The patient demonstrated symptoms after a month with persistent cough and fever.

Case 2 and 3 were two Chinese tourists who traveled together to France. Both of them visited a hospital in Wuhan as case 3 had a medical condition that was not relevant to COVID-19 disease. On the day they arrived, case 2, a 31-year old man, developed fatigue, fever, conjunctivitis, chills, and cough. Case 3, a 30-year old woman, also presented similar symptoms except for conjunctivitis 4 days later. On the 6th day of their arrival, they contacted the national hotline on the advice of the China embassy. They were immediately transferred to a regional referring hospital and isolated and sampled for laboratory confirmation of COVID-19. On the same day, it was confirmed that both of them were infected with SARS-CoV-2 (12).

Italy has been another country after China which was affected. The first two cases in Italy were a Chinese couple from Wuhan who entered Italy as tourists through Milan and traveled to Rome and accommodated in a hostel in the city center. They were admitted to a specialized hospital in infectious diseases. Not detailed information was provided in the published case report (13).

Turning to the Americas, in the United States has currently now the highest number of infected cases. The first infected patient with COVID-19 in the US was a 35-year-old man without any underlying condition who traveled to Wuhan with no visit to the wet market or health care facilities, and no contact with any confirmed patients with COVID-19. On the fourth day of his arrival to the US, he presented cough and subjective fever which lasted 4 days, and then he attended an urgent care clinic. The nasopharyngeal swab specimen tests returned negative for all pathogens test and her chest X-ray revealed no abnormalities. However, on the next day, the patient’s nasopharyngeal and oropharyngeal swabs were tested positive for 2019-nCoV by Reverse transcription polymerase chain reaction (RT-PCR) assay. The patient was admitted to a hospital in an airborne-isolation unit. His symptoms were dry cough, history of 2-day nausea and vomiting with no chest pain or shortness of breath and normal vital signs. The patient received supportive care and his signs appeared stable on the 2nd day of hospitalization, but he developed intermittent fevers along with tachycardia, diarrhea and abdominal discomfort. In addition, the non-productive cough and fatigue symptoms were continued. On the next day, the lungs radiography was normal. On day 6 the clinical symptoms improved, and atypical pneumonia was observed in the radiograph. The patient was well on day 8 and remained stable but hospitalized. All symptoms were managed except for a decreasing cough (14).

Canada was another country in Americas where a 56-year-old man with non-productive cough and fever and a well-controlled hyper blood pressure visited the Emergency Department in
Toronto. One day after he returned from Wuhan, a chest x-ray showed patchy bilateral, peribronchovascular, ill-defined opacities in all lung zones. Considering the clinical presentation of viral pneumonia in a patient with the appropriate epidemiological risk, the patient was admitted as a probable case of COVID-19. The results of the tests were negative for influenza virus A and influenza virus B, parainfluenza virus, respiratory syncytial virus, adenovirus, and human metapneumovirus. PCR showed COVID-19 in both mid-turbinate and throat swabs and sequencing confirmed the 2019-nCoV. One day after admission the patient remained well but developed mild haemoptysis and significant rhinorrhea and intermittent fever which lasted 5 days before it was completely managed. The patient discharged home and was on follow up assessments by public health workers. The authors concluded that patients with mild pneumonia who did not require supplementary oxygen and intubation could be isolated at their homes (15).

In summary, travel to Wuhan was the main reason for spreading the virus in these countries, regardless of exposure to the known risk factors including the wet market, live animal and sick people. The findings so far suggest that the disease starts with various initial symptoms, which is different from the original idea of manifestation of high body temperature and dry cough. It is not possible to consider a fixed set of symptoms for infected patients with the COVID-19. Further, in cases with negative nucleic acid testing and with a rapid progression of chest imaging, repeated nucleic acid testing is required to confirm the diagnosis of COVID-19. Another important finding was that none of these cases developed severe symptoms. They visited the hospitals as they had seen a health alert from the governments, or they were screened mainly at borders in the airports only because they were traveling. These results highlight the critical role of the early actions of governments and authorities to have policies in place with the purpose of providing valid information for the general population and inform the world without delay and control infection spread in such crises.

After the outbreak in China, Italy became the secondary source for spreading the disease with a rapidly increasing number of infected cases. Among Latin American countries, Brazil published a report of its first infected case. The first Brazilian case was a 61 years-old man with a 12-day travel history to Lombardy, Italy. On the first day of his arrival to Brazil he presented to the Hospital Albert Einstein in São Paulo, where his initial real-time RT-PCR was positive for SARS-CoV-2. The patient displayed dry cough, fever, coryza, and sore throat. He was isolated at home, received standard precautionary care, and presented mild signs one week after his arrival to Brazil (16).

It can be concluded that there might be several similar infected mild cases with COVID-19 with or without flu-like symptoms that have entered into different countries before the authorities started screening for probable infected cases. Considering virulence of the COVID-19, the potential cases contribute to beginning a rapid COVID-19 community transmission. This report emphasizes once more the importance of early action of the authorities in such global emergency situations.
Discussion

The outbreak of COVID-19 has currently gained a growing focus of the World Health Organization and all sectors around the world to minimize the deadly effects of the disease globally. We reviewed the first cases with COVID-19 reported by 10 countries with a focus on travel history to China in order to suggest the strategies that ensure minimizing the spread of the disease. The findings of this study suggest that the lack of prompt action in closing the borders was the main reason for the huge spread of the disease. In support of this assumption, the first cases of 9 out of 10 countries were infected via residence in or travel to Wuhan in China. It should be considered significant that in metropolis cities the spread of contagious infections can be faster than other areas, therefore the place of epidemic can be affective factor on the development of the susceptible people e.g. in the United States and China the spread of COVID-19 can be faster (17). Also, the primary measure to reduce the spread of the COVID-19 is of great importance in which in the early phase of epidemic the spread of the infectious disease can be increased more and more (18).

One key factor in controlling the spread of the virus might be using reliable screening strategies in the borders. One of the methods was used in the past months since the pandemic started was measuring body temperature. The results of this review demonstrated that fever was not a definite indicator for diagnosing patients with COVID-19 as several cases did not develop a fever. The main clinical presentation of most of the reported cases was lower respiratory presentation such as caught, sore throat, and dyspnea, and lung infiltration in CT scan evaluation. In addition, mild cases did not display signs and symptoms except for flu-like symptoms. Missing these cases at the borders is most likely resulting in more infected cases in the communities.

Regarding the mild cases, it is possible that the mild symptoms particularly the ones which are not accompanied by shortness of breathing might not be taken seriously by the infected cases. These symptoms might be considered as a common cold or flu by them, while they live their normal daily routine and spread the virus in the communities. One possible strategy is providing people with early public health warnings about the outbreak and the possible early symptoms of the disease. Employing such a strategy also helps authorities in controlling the spread of the virus. One reason that the health authorities were not able to control the disease in a timely manner could be that some countries did not provide valid and timely information to the WHO. Therefore, having some regulation in place by the WHO can be an efficient strategy to ensure all health authorities across the world comply with the regulation and provide them with timely information about emerging deadly diseases. Developing such regulation is a pressing need for future similar situations to prevent entering a pandemic phase from an epidemic phase.

Another area of interest might be that most of these cases were diagnosed after clinical manifestation. However, a serologic study reported that a large number of infected cases did not
have any clinical presentations. Therefore, several asymptomatic cases have not been diagnosed and live their normal lives in communities while they were carriers. It remained unclear whether symptomatic or asymptomatic cases played a key role in spreading the disease (19).

Another critical level of controlling an infectious disease might be early identification and isolation of the new cases or instructing them for quarantine at home. The reported cases presented to the designated hospitals or clinics 5-9 days after the onset of their symptoms. This suggests that before attending the health clinics several individuals in the community were already infected by these new cases that still were not aware of their condition and attended various places around their cities, countries and most importantly other countries and committed to the transmission of the disease. What is important is the prevention of infection, which can be achieved to some extent by knowing how the early cases are infected. In fact, prevention is better than cure. There are many different treatments for COVID-19 today (20), but no definitive cure has been found and sometime antiviral drugs used to treat COVID-19 have renal and liver complications (21). Treatment is much more complicated than follow-up. One interesting finding of this review was that early detection of pneumonia without clinical features may stop the development of severe pneumonia and admission to the intensive care unit. Thus, rapid diagnostic strategies ensure decreasing the spread of disease. To do so the health authorities will need to focus on clinical research for rapid, cost-effective and simple screening of pneumonia for similar future crises.

Conclusion

In conclusion, no consistent set of symptoms was found. However, flu-like symptoms were found to be predictors of new cases. The lack of typical pneumonia is not a reason for postponing chest X-ray or CT scan as there were cases that were diagnosed only because of the early chest CT scans that showed early stages of pneumonia. From a policy-making point of view, analyzing and understanding which strategies are optimal in the prevention of infectious diseases may help to achieve better results in the future. This warrants further investigation and analyzing the lessons taken from the COVID-19 pandemic. Regarding the mild cases, it is possible that the mild symptoms particularly the ones which are not accompanied by shortness of breathing might not be taken seriously by the infected cases.

Conflict of interest

The authors declare that they do not have conflict of interest.

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Declaration of competing interest

The authors report no conflicts of interest.

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