

The COVID-19 Outbreak in Iran: Its Lessons for Us

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Abstract

SARS-CoV-2, with 96% genetic similarity to the bat coronavirus transmitted to humans by the intermediate host in China, has been spread rapidly by travelers to most countries, including Iran. Following the detection of the first death related to COVID-19 on February 19, 2020, in the health center of Qom, a holy city in the center of Iran, the spread of the virus in Iran was initiated and quickly spread to all provinces of Iran by asymptomatic individuals. Until April 21, 2020, of the 330 137 tested patients, the number of infected people was 80,868. The most common clinical symptoms were fever, cough, fatigue, and dyspnea. Patients had abnormal computed tomography scans, lymphopenia, and elevated C-reactive protein. The patients and those who were in contact with them had to be quarantined. Other asymptomatic people also recommended quarantining themselves at home to cut off the transmission chain. Therefore, COVID-19 could be controlled by disinfecting public places, informing people, providing comprehensive assistance to stay at home, and most importantly, initiating vaccination.

Keywords: SARS-CoV-2, COVID-19, Transmission, Quarantine

Introduction

Coronaviruses are zoonotic and tend to move from one animal to another.¹ They usually cause a mild infection of the upper respiratory tract in humans. In recent years, a modified coronavirus has been transmitted from bat to civet. Then, it spread to humans and caused severe acute respiratory syndrome (SARS) between 2002 and 2003, with a mortality rate of 10%.² Ten years later, the coronavirus was transmitted from bat to camel and eventually to humans, which caused Middle East respiratory syndrome (MERS) with a mortality rate of 35%.³ Iran was also one of those countries.⁴ In December 2019, several people developed pneumonia without a cause in Wuhan, Hubei Province, China. Most of them had been to the seafood market, where live animals were traded.⁵ A novel coronavirus (2019-nCoV) was isolated from these patients, which was identified as the causative agent of COVID-19. The virus could be transmitted from one human to another.⁶ In some people, it could cause acute respiratory distress syndrome (ARDS), and in some old patients with underlying diseases, it could cause death.⁷ This review considered the etiology, clinical signs, host immune response, genetics, transmission, diagnosis,

control, epidemiology, and prevalence of COVID-19 in Iran. In addition, it investigated Iranian preventive behaviors during an outbreak of COVID-19 in Iran that helped make preventive decisions to reduce the disease in Iran and worldwide.

Etiology

2019-nCoV was the etiologic agent of pandemic acute respiratory syndrome in 2020, which has been named by Chinese researchers. Afterward, the International Committee on Taxonomy of Viruses named it SARS-CoV-2. Coronaviruses belong to the family Coronaviridae, a subfamily of Orthocoronavirinae. These viruses are large (120–160 nm). They are non-segmented positive-sense single-stranded RNA viruses and have spike-like protrusions that are spaced apart.⁸ Based on phylogenetic relationships and genomic structure, Coronavirinae has four genera, including alpha, beta, gamma, and delta groups, and can cause persistent infections in animals.¹ So far, seven types of coronaviruses have been identified that cause infections in humans, including NL63, 229E, OC43, HKU1, MERS-CoV, SARS-CoV,⁹ and SARS-CoV-2. The genome size of SARS-CoV-2 is 29891n, with 79.5%



sequence similarity to SARS-CoV.⁵ The genetic similarity to MERS-CoV is about 50%,¹⁰ while its similarity to bat coronavirus is 96%.⁵ Coronaviruses 229E, OC43, NL63, and HKU1 cause mild upper respiratory disease and rarely can cause severe infection in children, adults, and immunocompetent hosts,¹¹ whereas SARS-CoV, MERS-CoV, and SARS-CoV-2 cause SARS.¹² Bats are hosts of a range of viruses and have the potential to create new coronaviruses with greater invasion or transmission potential because of their specific immune system, high number, long life span, and ability to fly.⁸ The primary source of SARS-CoV-2 was a bat, considering that a nucleotide substitution mutation has occurred in genes related to structural and nonstructural proteins of the bat SARS-related coronavirus (SARSr-CoV),^{13,14} especially in the S gene encoding the spike (S) protein.¹⁵ These mutations affect their transmission rate and severity of infection. Similar to SARS-CoV, the virus binds to target cell surface receptors, the angiotensin-converting enzyme 2 (ACE2) receptors, via its spike glycoproteins.^{5,16} Altered viruses are transmitted to other animals, such as snakes¹⁷ or minks via fecal-oral.¹⁸ The virus may be more affected by mutations in their bodies, and SARS-CoV-2 was transmitted directly via air or infected surfaces to humans in the Huanan seafood market in Wuhan, China.¹⁹

Epidemiology

COVID-19 has rapidly spread in Iran and many countries worldwide. Until March 27, 2019, the total number of positive cases in the world reached 509,164 cases, and there were positive reports from 205 countries, with the USA having the highest incidence of disease, followed by Spain, Italy, Germany, France, Iran, and the UK.²⁰ Iran officially announced the COVID-19 outbreak in the country after the detection of the first death related to COVID-19 on February 19, 2020, in Qom, a holy city in the center of Iran. After a short time, COVID-19 spread widely in all provinces of Iran. Until 21, 2020, of the 330 137 tested patients, the number of infected people was reported to be 80 868 individuals.²¹ However, in some cases, there have been fluctuations because of the lack of a diagnostic kit. Iran was one of the first infected countries to experience the rapid progression of the pandemic. At the end of March 2020, the first peak occurred in late March 2020. The population of daily cases was around 3200 individuals, which led to a challenging situation for treatment staff and society.²² Iran faced many problems with providing personal protective equipment and, most importantly, hospital and laboratory equipment because of global supply shortages following the rapid spread of the COVID-19 infection. Restrictions on payments through the international banking system added to this challenge.²³ As of January 2022, the Iranian population had experienced five consecutive waves of COVID-19 infection in its epidemiological curve. The speed of virus transmission was successfully mitigated by implementing disease control policies at different stages of the epidemic.

However, with the progress of the pandemic, confronting virus infection became challenging because of the vast waves in passing time. The COVID-19 epidemic in Iran had a remarkable effect on social life, with over seven million confirmed infected cases and approximately 140 thousand confirmed death tallies to date.^{24,25} Up to now, unbelievable insight has been discovered into COVID-19, but studies offering an overall view of the pandemic have mainly dominated it.²⁶⁻²⁸

Transmission

COVID-19 is a zoonotic disease, and its agent was probably transmitted to humans by an intermediate host such as minks in the Huanan seafood market. Then, it was spread among the Chinese by human-to-human transmission.²⁹ It quickly moved from China to many countries, including Iran, creating the first pandemic of the 21st century. China's rapid release of COVID-19 happened because of the widespread relocation of people during the Lunar New Year holiday in early 2020.³⁰ It should be noted that the duration of this holiday was much shorter than the incubation period for COVID-19.³¹ Congestion in trains, buses, and airplanes has caused infected people to have multiple close contacts over long distances with other people, causing infection. Regarding the cause of the outbreak in Iran, it is possible that in Qom, a person or persons who were initially infected were suspected to have seasonal influenza, which was common. They referred to government-specialized clinics that cost much less than other centers. In addition, long waiting times (on average, two hours) to visit a physician in crowded and relatively small clinics resulted in the transmission of the virus to other clients. Then, the newly infected people in Qom spread the infection through gatherings in the shrine of Hazrat-e Masoumeh (peace be upon her), mosques, shops, and supermarkets.

Viruses usually spread in the same way they enter the body, and their release depends on the number of infected people, the transmissibility of the infection, and the clinical severity of the disease. The virus has high transmissibility, and its reproduction number (R0) was higher than the SARS and MERS viruses (about 2.2).⁶ Thus, the virus was transmitted from human to human through tiny droplets during sneezing, coughing, and discharging of nasal and oral secretions. Individuals also get infected by contact with contaminated surfaces such as tables, chairs, stair railings, door handles, and banknotes. However, it was observed that in addition to COVID-19 patients, who are the primary source of infection, asymptomatic patients could infect other people.³² Considering that COVID-19 was an emerging disease, early diagnosis was difficult for Iranian physicians and all countries. As a result, patients referred to clinics and patients admitted to hospitals infected other patients and health workers through close contact and caused death in some (unpublished data).³³

The most important way to transmit SARS-CoV-2 was through popular gatherings and, therefore, ceremonies

such as funerals, mourning, and weddings. The virus behaved unknowingly, and it was too early to predict how the virus would function in hot weather. Moreover, it might not be eliminated in hot weather and thus become endemic, similar to MERS-CoV.³⁴ In that case, it was likely at the time of the Hajj pilgrimage on July 31, 2020; the virus spread to Mecca and Medina and became an enormous threat to the pilgrims. Most people who go to the Hajj al-tamattu because of the long waiting times are often older than most people. Generally, elderly people with underlying diseases such as heart and lung diseases, diabetes, and hypertension were more likely to be infected with SARS-CoV-2. Therefore, the Hajj was abolished during the pandemic of the SARS-CoV-2 infection.

Clinical Characteristics

In individuals infected with SARS-CoV-2, clinical symptoms vary depending on the strength of the individual's immune system and the location of the virus in the upper or lower respiratory tract. In people with strong immune systems, it could be like a simple cold with mild symptoms of the upper respiratory tract, in some people, it caused pneumonia, and in others, it caused ARDS and respiratory failure.³⁵ According to studies including 1,721 people in China and Singapore,^{7,31,36-42} 57.7% of infected people were male, and patients were distributed in different age groups as ≥ 14 years (1%), 15-49 (52.2%), 50-64 (31%), and ≤ 65 (15.8%). The most common clinical symptoms were fever (98.8%), cough (68.3%), fatigue (39.1%), sputum production (33.8%), dyspnea (32.7%), shortness of breath (18.5%), loss of appetite (17.6%), myalgia (14.3%), sore throat (13.6%), headache (13.4%), anorexia (12.2%), chills (11.5%), nausea and vomiting (6.9%), diarrhea (5.3%), rhinorrhea (4.2%), and hemoptysis (1.2%). Among infected individuals, 87.9% showed abnormal chest computed tomography (CT) scans, usually with bilateral lung involvement. In a study, only 5 cases (2.9%) with normal CT scans were detected among the patients with severe disease.³¹ Laboratory findings revealed that 36.7% and 78.2% of patients had leukopenia and lymphopenia, respectively. Lymphopenia determines the severity of the infection.⁴³ However, leukocytosis was observed in patients with severe pneumonia (6.7%) rather than leukopenia, especially in those with secondary infection. Elevated levels of C-reactive protein (65.6%), D-dimer (46%), lactate dehydrogenase (41.5%), aspartate aminotransferase (22.4%), alanine aminotransferase (21.3%), and procalcitonin (11.2%) were detected in the cases. Among COVID-19 patients, 31% had at least one underlying disease. The underlying diseases included hypertension (17.4%), diabetes mellitus (8.3%), chronic cardiac disease (6.4%), chronic liver disease (3%), malignancy (1.6%), cerebrovascular disease (1.5%), chronic pulmonary disease (1.3%), chronic renal disease (1%), and immunodeficiency (0.2%), respectively. ARDS was the most common complication (6.8%) in the patients. The mortality rate was about 2.6%, which was

higher in older adults.^{7,31,36-42,44}

Diagnosis of COVID-19

The initial diagnosis was based on clinical symptoms, and a definitive diagnosis was possible based on laboratory and radiological results. The most appropriate way to identify viruses was using the cell culture method. Vero cells were used for virus isolation and final sequencing.⁴⁵ Considering that the virus culture process is time-consuming and requires a biosafety level-3 laboratory, it is unsuitable for diagnosis in the epidemic. Then, the presence of the virus in the body was determined by real-time polymerase chain reaction (RT-PCR), and the most appropriate specimen for severe cases was bronchoalveolar lavage fluid. The results of the RT-PCR test varied from 43% to 89% positive in patients.⁴⁶ In a study on 1014 patients, 59% of the cases were positive by RT-PCR, and the rest had negative results. However, a chest CT scan could detect 88% of patients.⁴⁷ The chest CT scan appears to be more sensitive to detecting COVID-19 than RT-PCR. CT scans became a top priority for the diagnosis of the disease in Iran and other countries. In addition, SARS-CoV-2 infection was detected by searching for specific antigens in biological samples, and antibody detection in the serum would be the most appropriate method to determine whether a person has been previously infected with the virus.

Immune Response

After the virus crosses the first line of defense, an immune system works to produce interferons against the virus to prevent the virus from proliferating. The proliferation of specific B and T lymphocytes of the virus produces SARS-CoV-2-binding immunoglobulin M/immunoglobulin G antibodies and increases activated CD4⁺ and CD8⁺ to control COVID-19.⁴⁸ In these individuals, symptoms of the SARS-CoV-2 infection are absent or very mild. Thus, an adequate and appropriate immune response was essential for controlling coronavirus, and the failure of the immune system during virus infection spread the infection. Nonspecific inflammatory responses caused edema, inflammatory cell infiltration, and exfoliation of alveolar epithelial cells,⁴⁹ leading to pneumonia, ARDS, respiratory failure, and possibly death. In a previous study, there was an increase in inflammatory biomarkers in patients with severe forms of COVID-19. The number of T, B, and natural killer cells decreased significantly, and the level of regulatory T cells that had the greatest effect on SARS-CoV-2 was also lower in more severe cases.⁵⁰ Therefore, it is likely that SARS-CoV-2 can affect T lymphocytes and produce inflammatory cytokines and lung tissue damage in immunocompromised individuals, similar to tuberculosis, which is more common in diabetic patients because of weakened immune systems.⁵¹ Therefore, strengthening the immune system by reducing stress, getting enough sleep, avoiding fatigue, and consuming enough fruits and vegetables, honey, milk,

and fish can protect the body against COVID-19 even if the SARS-CoV-2 virus has entered the body.

Control and Prevention

Because of the rapid transmission from human to human, SARS-CoV-2 has become a crucial global public health problem in a short time,^{6,29,52} and human gatherings could increase the risk of exposure and infection.⁵³ Virus transmission in the incubation period was up to 24 days,³¹ and in the recovery period, it was up to 13 days.⁵⁴ First, because of the lack of standard treatment and an effective vaccine for control and prevention, the best way was to cut off the transmission chain to reduce contact with infected people. The first step in this process was to isolate patients and quarantine people who had been in contact with them. Cancellation of trips⁵⁵ and any gatherings, whatever the case may be, could help break the chain of transmission of COVID-19. It was also essential to disinfect the streets and crowded places. Interestingly, unlike most viruses that cannot survive outside the body, it could survive for up to 28 days on stainless steel⁵⁶ and plastic, and glass for up to 9 days.⁵⁷ Therefore, it was necessary to disinfect public places. Healthcare workers are highly likely to become infected during endotracheal suction as well as the intubation, examination, and carrying of patients; therefore, sufficient protective equipment such as gloves, N95 masks, goggles, face shields, shoe covers, hand disinfectants, and gowns is demanded to be sufficiently available. The day-to-day activities of medical staff, especially physicians and nurses, cause sleepiness, fatigue, and stress, which leads to reduced immunity. To the best of our knowledge, gatherings in health centers and clinics have been the essential causes of the outbreak of COVID-19 in Iran.

People needed to pursue various steps to prevent infection and transmission, including (1) staying at home, leaving home only when it was necessary, and getting essential tasks performed by just one healthy person, (2) increasing the level of immunity with rest, adequate nutrition, and home exercise, (3) improving personal hygiene and environmental health, and (4) avoiding stress. The other steps are (5) avoiding public places, (6) not touching public objects and surfaces, (7) having a mask in meetings, (8) wearing gloves when shopping, (9) maintaining social distancing, (10) avoiding handshakes, (11) covering the mouth and nose during coughing and sneezing, (12) not touching the mouth and mucus, and (13) avoiding smoking and hookah. The remaining steps included (14) gargling with normal saline after returning home and before bedtime and (15) washing hands with soap and water when returning home, before cooking and eating, and after using the toilet. However, at the early outbreak phase, there were different challenges in various countries, especially Iran, to eradicate the disease, including (1) a lack of proper treatment and vaccine, therefore, an accurate understanding of the mechanism of lung injury was essential for treatment and reducing

mortality, (2) the presence of asymptomatic individuals in society, and (3) Nowruz, shopping, and visiting. The other challenges were (4) prioritization of treatment over prevention, (5) US sanctions and lack of personal protection and diagnostic equipment, (6) spreading misleading and fake news on social media by ignorant people, (7) psychological aspects of fear of the coronavirus that was increased its effects after controlling COVID-19, and (8) ignoring the outbreak of the disease by some people.

Lessons Learned

In Iran, health authorities have noticed the infection late in the country. This delay may be because of various factors, such as the priority of treatment in health and prevention, the prioritization of the personal interests of some authorities over the interests of the community, and the failure of some people to cooperate. As a result, unfortunately, COVID-19 has increased day by day. The prevalence of infection coinciding with the last months of the solar year and a culture of buying new clothes at the start of the new year among Iranians made people gather in the markets and spread the disease despite repeated health recommendations by social media. Efforts of the healthcare staff for self-quarantining and staying at home, especially those who had symptoms of a virus infection, and breaking the transmission chain could control the epidemic in Iran. The COVID-19 pandemic emphasized the deliberate importance of the industry of vaccine production in controlling disease and, most importantly, collective health. This pandemic created an enormous global demand for early vaccination. However, only a limited number of countries could produce the COVID-19 vaccine promptly, which highlights the importance of vaccine production as a strategic asset.⁵⁸

The study had some limitations. Statistics do not show all infected people in Iran and other countries because a significant number of people were asymptomatic and did not refer to medical centers. The definitive diagnosis method in Iran and many other countries was RT-PCR. Some COVID-19 patients have not been reported as positive because of inadequate sampling and defects in the kit and testing.

Conclusion

The findings revealed that the heavy air traffic between Iran and China facilitated the transmission of SARS-CoV-2 from China to Iran during the outbreak of the infection in China. Because of weaknesses in the management system of the Ministry of Health and Population in health centers and the implementation of a defective plan of per-case in these centers, the disease became an epidemic in Iran, which caused the deaths of a significant number of Iranian people. With the efforts of the Iranian government and nation, self-quarantine, careful attention to strict health measures, the extensive work of the healthcare staff, and most importantly, the COVID-19 vaccination, the disease

was controlled all over the world.

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Competing Interests

The authors declare no conflict of interests.

Ethical Approval

Not applicable

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