

## Review Article

# Challenges Presented by SARS-Corona Virus 2 to Global Health

Dr. Hasnatul Jannat<sup>1</sup>, Kazi Taib Mamun<sup>2</sup>, Dr. Nabeela Mahboob<sup>1</sup>, Dr. Hasina Iqbal<sup>1</sup>, Dr. Sabrina Afrin<sup>1</sup>

<sup>1</sup>Department of Microbiology, Popular Medical College, <sup>2</sup>Research Investigator, icddr.

### Abstract

Emerging and reemerging pathogens are global challenges for public health. In recent times, corona viruses have become the most important virus worldwide because of the occurrence of more than 2 thousand deaths caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China. Rapid spread of the infection occurred in many countries. However, most cases of mortality have occurred in China. The Center for Diseases Control and Prevention and World Health Organization maintain a website that is updated frequently with new cases of SARS-CoV-2 infection. Here we provide a brief introduction to corona viruses and also discuss the outbreaks of recently identified SARS-CoV-2.

**Key words:** Corona virus, SARS-CoV-2, COVID-19.

### Introduction:

Since the last decade, several life threatening viruses have emerged as a global threat. These viruses have been responsible for causing significant human mortality; in addition they have raised serious public health concerns worldwide. Various factors like modern life style, extensive travel of humans and goods, deforestation have been implicated for the spread and emergences of these viruses. Thus, their outbreak anywhere in the world is potentially a risk for the whole world.<sup>1</sup> At present, due to high genomic nucleotide substitution rates and recombination, Human Coronaviruses (HCoVs) are considered as one of the most rapidly emerging viruses.<sup>2</sup> HCoVs consists of a major group of coronaviruses (CoVs) which are responsible for multiple respiratory diseases of varying severity, including common cold, pneumonia and bronchitis.<sup>3</sup> To date, seven strains of HCoVs have been isolated, namely HCoV-229E, HCoV-NL63, HCoV-OC43, CoV-HKU1, severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and 2019 Novel coronavirus (2019-nCoV). People all over the world commonly get

infected with HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoV-HKU1. Coronaviruses that infect animals can evolve and cause human diseases and become a new human coronavirus. Three recent examples of these are 2019-nCoV, SARS-CoV, and MERS-CoV.<sup>4</sup> The recent outbreak of viral pneumonia cases due to a 2019-nCoV in the Wuhan poses significant threats to public health and has grown new interest in human coronaviruses around the world.<sup>5</sup>

### History of the corona virus

Corona virus was first identified as a cause of the common cold in 1968.<sup>6</sup> Prior to the SARS-CoV outbreak, coronaviruses were only thought to cause mild, self-limiting respiratory infections in humans. Two of these human coronaviruses are  $\alpha$ -coronaviruses (HCoV-229E and HCoV-NL63) while the other two are  $\beta$ -coronaviruses (HCoV-OC43 and HCoV-HKU1). HCoV-229E and HCoV-OC43 were identified nearly 50 years ago.<sup>7,8</sup> while HCoV-NL63 and HCoV-HKU1 were identified following the SARS-CoV outbreak.<sup>9</sup> These viruses are endemic in the human populations, causing 15-30% of respiratory tract infections each year. They cause more severe disease in neonates, the elderly and in individuals with underlying illnesses, with a greater incidence of lower respiratory tract infection in these populations. HCoV-NL63 is also associated with acute laryngotracheitis (croup).<sup>10</sup>

Prior to the outbreak by 2019-nCoV, two novel viruses were implicated to be responsible for severe acute illness

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### Correspondence:

**Dr. Hasnatul Jannat**

Lecturer

Department of Microbiology

Popular Medical College, Dhaka.

Contact No: 01673008869

Email: hasnatuljannatszmc17@gmail.com

i.e. Middle East Respiratory Syndrome-Corona-Virus (MERS-CoV) and severe acute respiratory syndrome-corona-virus (SARS-CoV).<sup>11,12</sup> Severe Acute Respiratory Syndrome (SARS) coronavirus first identified in China in 2003, causing atypical pneumonia marked by fever, headache and subsequent onset of respiratory symptoms such as cough and pneumonia, which later developed into life-threatening respiratory failure and acute respiratory distress syndrome.<sup>13</sup> Originally, palm civets were thought to be the natural reservoir for the virus.<sup>14</sup> However, subsequent phylogenetic studies confirmed the bat origin of SARS-CoV based on sequences of SARS-like virus found in bats.<sup>15</sup> While the SARS-CoV epidemic was controlled in 2003 and the virus has not since returned.

The Middle East Respiratory Syndrome (MERS) Coronavirus (MERS-CoV), a lethal zoonotic pathogen that was first identified in humans in the Kingdom of Saudi Arabia (KSA) in 2012 continues to emerge and re-emerge through intermittent sporadic cases, community clusters and nosocomial outbreaks. Humans acquire MERS-CoV infection probably through contact with camels or camel products while nosocomial transmission is also a hallmark.<sup>16</sup> The evolution of this virus demonstrated that coronavirus is not a stable virus and can adapt to become more virulent, even lethal to humans.

### SARS-Coronavirus-2

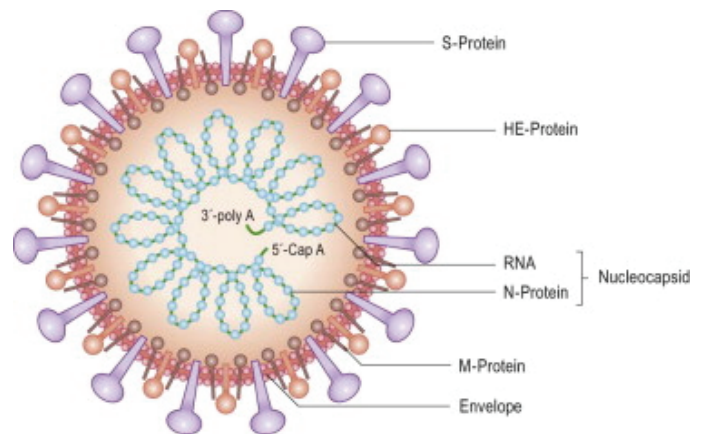
Recently, the city of Wuhan in China is the focus of global attention due to an outbreak of a febrile respiratory illness caused by a coronavirus. In December 2019, there was an outbreak of pneumonia of unknown cause in Wuhan, Hubei province in China, with an epidemiological link to the Huanan Seafood Wholesale Market where there was also sale of live animals.<sup>17</sup> Following this outbreak considering the shared history of exposure to Huanan seafood market across the patients, an epidemiological alert was released by the local health authority on Dec 31, 2019 and the market was shut down on January 1, 2020.<sup>18</sup> Deep sequencing analysis from lower respiratory tract samples indicated a novel coronavirus and this has facilitated the laboratories in different countries to produce specific diagnostic PCR tests for detecting the novel infection.<sup>19</sup> On 10 January 2020, the first novel coronavirus genome sequence was made publicly available. The sequence was deposited in the GenBank database (accession number MN908947).<sup>20</sup> On 30 January 2020, 2019-nCoV was designated a public Health Emergency of International Concern by the WHO.<sup>21</sup>

2019-nCoV is a  $\beta$  CoV of group 2B with at least 70% similarity in genetic sequence to SARS-CoV. On

February 11, 2020, the International Committee on Taxonomy of Viruses, named the novel coronavirus, first identified in Wuhan, China as severe acute respiratory syndrome coronavirus 2, shortened to SARS-CoV-2 formerly known as 2019-nCoV.<sup>22</sup> and on the same day World Health Organization announced an official name for the disease that is causing the 2019-nCoV outbreak, first identified in Wuhan China. The new name of this disease is coronavirus disease 2019, abbreviated as COVID-19.<sup>23</sup>

### Taxonomy, Genomic Structure and Morphology

CoVs are a group of large single stranded enveloped RNA viruses belonging to the family Coronaviridae. Along with Artieriviridae and Roniviridae, Coronaviridae is classified under the Nidovirales order.<sup>24</sup> Based on sequence comparisons of entire viral genome, CoVs are further categorized into four main genera, Alpha, Beta, Gamma and Delta coronaviruses by the International Committee for Taxonomy of Viruses.<sup>22</sup> These viruses were first identified in 1968 and got their name from the “corona” like or crown like morphology observed under the electron microscope.<sup>6</sup> They contain a non-segmented, positive-sense RNA genome of ~30 kb. Two-thirds of the genome, about 20 kb are occupied by the replicase gene encoding the nonstructural proteins (Nsps) whereas structural and accessory proteins consist of only about 10 kb of the viral genome.<sup>25</sup> Four main structural proteins that contribute to produce a complete viral particle are the spike (S), membrane (M), envelope (E), and nucleocapsid (N).<sup>26</sup>



**Figure-I:** Structure of Coronavirus

### Epidemiology

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first emerged in December 2019 in China. Since its emergence, a total of 79331 patients from 30 countries have been infected across the globe

according to a World Health Organization (WHO) report. Approximately 2618 patients have died.<sup>27</sup> Severe acute respiratory syndrome (SARS) is a zoonotic disease caused by SARS-CoV, which first emerged in 2002 in China. Consequently, as many as 8273 cases were confirmed from 37 countries around the world with a mortality rate of about 10% due to its high transmissibility among humans.<sup>28</sup> The MERS-CoV epidemic occurred in Saudi Arabia in 2012 with similar clinical symptoms as SARS-CoV but with a much higher mortality rate of about 35%.<sup>29</sup> Unlike SARS-CoV, which exhibits super-spreader events, transmission of MERS-CoV is geographically limited.<sup>30</sup>

### Transmission

Coronaviruses were originally found as enzootic infections, limited only to their natural animal hosts, but have crossed the animal-human species barrier and progressed to establish zoonotic diseases in humans.<sup>31</sup> Early on, outbreak of respiratory illness caused by SARS-CoV-2 in Wuhan, suggesting animal-to-person spread. Later, a growing number of patients reportedly did not have exposure to animal markets, indicating person-to-person spread. Chinese officials report that sustained person-to-person spread in the community is occurring in China and also outside China, including in the United States and other countries. Transmission occurs between people who are in close contact with one another (within about 6 feet), via respiratory droplets produced when an infected person coughs or sneezes, touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes, but this may not be the main way the virus spreads<sup>4</sup>. According to Chinese researchers, the coronavirus is also shed in the feces of infected people causing faecal-oral transmission, which may help explain why it's spread so fast.<sup>32</sup>

A super-spreader is an unusually contagious organism infected with a disease. In context of a human-borne illness, a super-spreader is an individual who is more likely to infect others, compared with a typical infected person.<sup>33</sup> Such super-spreaders may be attributed for the sudden jump of SARS-CoV-2 in South Korea. According to a news reports, a so-called super-spreader woman infected at least 37 people at her church with the new coronavirus, and dozens of additional worshippers are also showing symptoms of the disease.<sup>34</sup> A super-spreader British man in the UK also has spread the virus to 11 other people.<sup>35</sup> So, like SARS-CoV where super-spreading events represented one of the most particular features of outbreak, these may also important factors for SARS-CoV-2 rapid spread.<sup>36</sup>

### Reservoir

Animals sold for food were originally suspected to be the reservoir or intermediary hosts of SARS-CoV-2 because many of the first individuals found to be infected by the virus were workers at the Huanan Seafood Market.<sup>5</sup> The current most likely hypothesis is that an intermediary host animal has played a role in the transmission.<sup>37</sup> However, some researchers have suggested that the Huanan Seafood Market may not be the original source of viral transmission to humans.<sup>38</sup> To be noted that serological studies conducted in rural population living close to bats natural habitat in caves revealed a 2.9% bat-CoV seroprevalence, demonstrating that humans exposure to bat-CoVs might be common.<sup>39</sup> Furthermore, it was found that 2019-nCoV is 96% identical at the whole-genome level to a bat coronavirus.<sup>40</sup>

### Clinical presentation

SARS-CoV-2 may present with mild, moderate, or severe illness; the latter includes severe pneumonia, ARDS, sepsis, septic shock and death.<sup>41</sup> Initial symptoms may present as simple flu like with fever, cough and shortness of breath. CDC believes at this time that symptoms of COVID-19 may appear in as few as 2 days or as long as 14 days after exposure.<sup>4</sup> 2-10% of patients with COVID-19 have had gastrointestinal symptoms such as diarrhoea, abdominal pain, and vomiting before the development of fever and respiratory symptoms.<sup>42</sup> The mechanism for gastrointestinal tract infection of SARS-CoV-2 is proposed to use the angiotensin-converting enzyme 2 (ACE2) cell receptor as its host receptor, but uses human ACE2 more efficiently than the 2003 strain of SARS-CoV.<sup>43</sup>

### Case definitions for surveillance

**Suspect case:** A. Patient with severe acute respiratory infection (fever, cough, and requiring admission to hospital) and with no other etiology that fully explains the clinical presentation and a history of travel to or residence in China during the 14 days prior to symptom onset, OR

B. Patient with any acute respiratory illness and at least one of the following during the 14 days prior to symptom onset:

a) contact with a confirmed or probable case of 2019-nCoV infection, OR

b) worked in or attended a health care facility where patients with confirmed or probable 2019-nCoV acute respiratory disease patients were being treated.

**Probable case:** A suspect case for whom testing for 2019-nCoV is inconclusive or is tested positive using a pan-coronavirus assay and without laboratory evidence of other respiratory pathogens.

**Confirmed case:** A person with laboratory confirmation of 2019-nCoV infection, irrespective of clinical signs and symptoms.

**Definition of contact:** A contact is a person involved in any of the following:

- Providing direct care for 2019-nCoV patients, working with health care workers infected with novel coronavirus, visiting patients or staying in the same close environment of a 2019-nCoV patient.
- Working together in close proximity or sharing the same classroom environment with 2019-nCoV patient
- Traveling together with 2019-nCoV patient in any kind of conveyance
- Living in the same household as a 2019-nCoV patient within a 14-day period after the onset of symptoms in the case under consideration.<sup>44</sup>

### Diagnosis

In most cases of self-limited infection, diagnosis of coronaviruses is unnecessary that causes mild illness. However, it is important in certain clinical and or in epidemiological studies to identify an etiological agent. Diagnosis is also important to locate the place where a severe CoV outbreak is occurring, such as, at present, in China, where SARS-CoV-2 continues to circulate.<sup>45</sup> Since the cause was unknown at the onset of this emerging infection, the diagnosis of pneumonia of unknown cause in Wuhan was based on clinical characteristics, chest imaging, and the ruling out of common bacterial and viral pathogens that cause pneumonia.<sup>18</sup>

Any person fulfilling the criteria for a suspected case should be tested for SARS-CoV-2. WHO recommends that lower respiratory specimens (sputum, endotracheal aspirate, or bronchoalveolar lavage) have a higher diagnostic value than upper respiratory tract specimens (nasopharyngeal swab, oropharyngeal swab, nasopharyngeal aspirate or nasal wash) for detecting SARS-CoV-2 infection. If collection of lower respiratory specimens is not possible, upper respiratory tract specimens should be collected. If initial testing is negative in a patient who is strongly suspected to have novel coronavirus infection, multiple respiratory tract sites specimen (nose, sputum, endotracheal aspirate) should be collected. Additional specimen may be collected such as blood, urine, and stool. When serological assays become available, WHO recommends that a paired acute and convalescent sera for antibody detection should also be collected.<sup>46</sup>

The genetic sequence of the SARS-CoV-2 has also become available to the WHO on 12 January 2020 and this has facilitated the laboratories in different countries

to produce specific diagnostic PCR tests for detecting the novel infection.<sup>46</sup> CDC has developed a new laboratory test kit for use in testing patient specimens for SARS-CoV-2. The test kit is called the “Centers for Disease Control and Prevention (CDC) 2019-nCoV Real-Time Reverse Transcriptase (RT)-PCR Diagnostic Panel”. CDC is supporting global efforts to study and learn about the virus that causes COVID-19 in the laboratory is by growing the virus in cell-culture so that researchers can use the virus in their studies.<sup>4</sup> A high index of suspicion, detailed exposure travel history and bilateral ground-glass opacities or consolidation at chest imaging should be considered to suggest SARS-CoV-2 as a possible diagnosis where short on test kits. Furthermore, a normal chest CT scan does not exclude the diagnosis of 2019-nCoV infection.<sup>47</sup>

### Treatment and Prevention

To date, there are no FDA-approved vaccines or anti-viral therapeutics that specifically target human coronaviruses. In the initial stages of the disease protease inhibitors such as lopinavir or ritonavir along with ribavirin may help in antiviral therapy.<sup>48</sup> COVID-19 with mild illness, hospitalization may not be required unless there is concern for rapid deterioration. All patients discharged home should be instructed to return to hospital if they develop any worsening of illness.<sup>49</sup> Given the emergence of the SARS-CoV-2 pneumonia cases during the influenza season, antibiotics and oseltamivir are empirically administered. Corticosteroid therapy is given as a combined regimen if severe community-acquired pneumonia is diagnosed by physicians at the designated hospital. Oxygen support (e.g, nasal cannula and invasive mechanical ventilation) is administered to patients according to the severity of hypoxaemia. Repeated tests for SARS-CoV-2 are done in patients confirmed to have SARS-CoV-2 infection to show viral clearance before hospital discharge or discontinuation of isolation.<sup>18</sup>

Due to the lack of effective therapeutics or vaccines, the best measures to control human coronaviruses remain a strong public health surveillance system coupled with rapid diagnostic testing and quarantine or isolation when necessary.<sup>50</sup> The best way to prevent illness is to avoid close contact with people who are sick, touching mouth, nose, and eyes; staying home when sick, avoid unprotected contact with farm or wild animals, always wash hands often with soap and water for at least 20 seconds, especially after direct contact with ill people or their environment. If soap and water are not readily available, use an alcohol-based hand sanitizer with at least 60% alcohol. People with symptoms of respiratory infection

should practice cough etiquette (maintain distance about 6 feet, cover coughs and sneezes with disposable tissues or clothing, and wash hands). Use facemasks by people who show symptoms of COVID-19 to help prevent the spread of the disease to others. The use of facemasks is also crucial for health workers and people who are taking care of someone in close settings (at home or in a health care facility).<sup>4</sup>

### Conclusion

The emergences of SARS-CoV, MERS-CoV and SARS-CoV-2 demonstrate the importance of the *Coronaviridae* as emerging human pathogens. The Wuhan outbreak is a stark reminder of the continuing threat of zoonotic diseases to global health security. Viral surveillance studies of animal species, including bats, rodents and livestock, are essential to understand the potential human pathogens that exist in the environment before they can spill over. Therefore, there is a need to research these potential emerging viruses and also to develop broad-spectrum vaccination or therapeutic strategies to prepare for current and future emerging coronaviruses.

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