Chapter 1
Current Insight into the Novel Coronavirus Disease 2019 (COVID-19)

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Abstract SARS-CoV-2 is a novel strain of coronavirus that has not been previously identified in humans. It has been declared a pandemic and has infected at least 1,844,683 individuals and caused 117,021 deaths as of 14th April 2020. Transmission among humans occurs via close contact with an infected individual that produces respiratory droplets. Patients have been shown to undergo acute respiratory distress syndrome, which is defined as cytokine storm. The diagnosis relies on detection of nucleic acid, IgG/IgM antibodies, and a chest radiograph of the suspected individuals. The genome of SARS-CoV-2 is similar to other coronaviruses that comprise of ten open reading frames (ORFs). SARS-CoV-2 spike protein exhibits higher affinity to ACE2 receptor as compared with SARS-CoV. Repurposing drugs like favipiravir, remdesivir, chloroquine, and TMPRSS2 protease inhibitors have been shown to be effective for the treatment of COVID-19. Personal protective measures should be followed to prevent SARS-CoV-2 infection. In addition, a clinical trial of SARS-CoV-2 vaccine, mRNA-1273, has been started. This chapter provides a glimpse of advancements made in the area of SARS-CoV-2 infection by proving recent clinical and research trials in the field.

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1.1 Introduction

On 11 March 2020, the World Health Organization (WHO) declared severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a pandemic that causes novel coronavirus disease 2019 (COVID-19) (World Health Organization 2020a). By 14 April 2020, around 1,844,683 confirmed cases with 117,021 deaths were reported from at least 213 countries, areas, or territories (World Health Organization 2020b). SARS-CoV-2 is a novel strain of coronavirus that has not been previously identified in humans. Phylogenetic analysis suggests that SARS-CoV-2 might have emerged from the zoonotic cycle and rapidly spread by human to human transmission (Chan et al. 2020a). However, the exact source of SARS-CoV-2 has not been identified yet. Transmission among humans occurs via close contact with an infected individual that produces respiratory droplets while coughing or sneezing within a range of about 6 ft (Ghinai et al. 2020). Infected individuals have been reported with common clinical symptoms involving fever, nonproductive cough, myalgia, shortness of breath, as well as normal or decreased leukocyte counts (Fig. 1.1) (Zhang et al. 2020). In addition, severe cases of infection cause pneumonia, severe acute respiratory syndrome, kidney failure, and death (Zhao et al. 2020; Xiong et al. 2020). Even with the implementation of strong travel restrictions, a large number of individuals exposed to SARS-CoV-2 have been traveling internationally without being detected, leading to spread of the virus worldwide (Chinazzi et al. 2020). However, extensive measures have been implemented by outstanding public health action to reduce person-to-person transmission of SARS-CoV-2 (Fig. 1.2). In addition, the scientific fraternity worldwide has been continuously working on COVID-19 from the beginning by publishing the genome and developing highly specific diagnostic tools for the detection of SARS-CoV-2 infection.

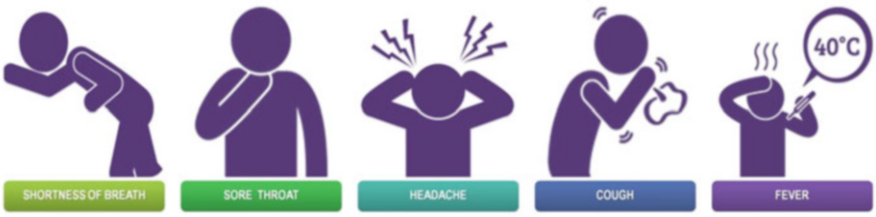

Fig. 1.1 Typical symptoms of COVID-19

Fig. 1.2 Personal protective measures to prevent SARS-CoV-2 infection

1.2 SARS-CoV-2 Genome and Pathogenesis

SARS-CoV-2 is a single-stranded RNA virus of ~30 kb genome size, which belongs to the genus *Coronavirus* and family Coronaviridae. The genome of SARS-CoV-2 is similar to other coronaviruses that comprise of ten open reading frames (ORFs). The first ORFs (ORF1a/b), about two-thirds of viral RNA, are translated into two large polyproteins pp1a and pp1ab, which processed into non-structural proteins (nsp1-nsp16) (Chan et al. 2020b). The size of each SARS-CoV-2 virion is about 70–90 nm (Kim et al. 2020). The genome of SARS-CoV-2 encodes for four structural proteins similar to other coronaviruses. These proteins are S (spike), E (envelope), M (membrane), and N (nucleocapsid) protein which are required to make complete virus particle. S protein is responsible for the attachment and entry of SARS-CoV-2 to the host target cell receptor, probably angiotensin-converting enzyme 2 (ACE2) mainly expressed on alveolar epithelial type II (AECII) cells, including extrapulmonary tissues such as heart, kidney, endothelium, and intestine (Yan et al. 2020). SARS-CoV-2 has been shown to exhibit novel glycosylation sites in the spike glycoprotein of 2019-nCoV, suggesting that the virus may utilize different glycosylation sites to interact with its receptors (Kumar et al. 2020). Studies have demonstrated that SARS-CoV-2 spike protein has higher affinity to the ACE2 receptor as compared with SARS (Walls et al. 2020).

1.3 Host Immune Response Against SARS-CoV-2

Upon entry into the host target cells, the viral antigens get presented via antigen-presenting cells (APCs) to virus-specific cytotoxic T lymphocytes (CTL). So far, studies have not been conducted that reveal the peptide presentation. However, CTL epitopes of SARS-CoV-2 have been predicted by several studies, which may be used for understanding the pathogenesis and development of peptide-based vaccines (Kumar et al. 2020; Walls et al. 2020). Studies have been conducted in SARS-CoV-2 infected patients showing the activation and reduction in $CD4^+$ and $CD8^+$ T cell counts (Li et al. 2020a). In addition, SARS-CoV-2 patients have been found to present with acute respiratory distress syndrome (ARDS) (Zumla et al. 2020). ARDS

is a cytokine storm syndrome (CSS) which is a lethal uncontrollable inflammatory response resulting from the release of large pro-inflammatory cytokines (IL-1β, IFN-α, IFN-γ, IL-12, IL-6, IL-18, TNF-α, IL-33, TGFβ, etc.) and chemokines (CCL3, CCL2, CXCL8, CCL5, CXCL9, CXCL10, etc.) by immune cells (Li et al. 2020a).

1.4 Diagnosis of Human SARS-CoV-2 Infection

Suspected patients get diagnosed for SARS-CoV-2 infection by collecting various specimens, including nasopharyngeal or oropharyngeal swabs, nasopharyngeal or oropharyngeal aspirates or washes, bronchoalveolar lavage, sputum, tracheal aspirates, and blood. Specimens can be stored at 4 °C for up to 72 h after sample collection and may be stored at −70 °C for longer periods of time (Centre for Disease Control and Prevention 2020a). Diagnosis tests such as nucleic acid test, ELISA, CT scan, and blood cultures are being implemented for the detection of SARS-CoV-2 infection. Commonly used nucleic acid tests are RT-qPCR and high-throughput sequencing, where RT-qPCR is the effective and straightforward method for detection of pathogenic viruses in respiratory secretions and blood. Specific primers and probes against ORF1ab and N gene regions have been recommended to use for the detection of SARS-CoV-2 (Wang et al. 2020a). In addition, immunological detection of IgM and IgG antibodies are being performed to diagnose the COVID-19 patients (Li et al. 2020b). Patients reporting respiratory discomfort were evaluated using CT scan (Zhou et al. 2020).

1.5 Treatment and Drugs for SARS-CoV-2

There is no specific treatment available for SARS-CoV-2 and the current treatment relies on supportive care of the infected patients (Centre for Disease Control and Prevention 2020b). However, some evidences suggest the use of repurposing drugs as the current choice of therapy. Remdesivir, a nucleoside analogue-based drug that is currently under clinical trial for treating Ebola virus infection, has been shown to block SARS-CoV-2 infection in vitro (Wang et al. 2020b). In addition, favipiravir, a type of RNA-dependent RNA polymerase inhibitor that has been designed to treat influenza virus infection, has been found to exhibit antiviral activity against SARS-CoV-2 (Dong et al. 2020). Use of chloroquine, especially hydroxychloroquine, has been found to be effective against SARS-CoV-2 in vitro, which interferes with the glycosylation of cellular receptors (Yao et al. 2020). Apart from attachment inhibitors, TMPRSS2 protease inhibitors have also been found to block SARS-CoV-2 infection in lung cells (Hoffmann et al. 2020).

Fig. 1.3 Steps needed to be taken by COVID-19 patients in order to prevent the spread of SARS-CoV-2 infection

1.6 Prevention and Control Strategies for SARS-CoV-2 Infection

The current preventive strategies of SARS-CoV-2 infection relies on personal protective measures such as covering of nose/mouth when coughing or sneezing, use of FFP3 or N95 mask, use of tissues to contain respiratory secretions and dispose of these in nearest waste receptacle, and hand hygiene after contact with contaminated objects/materials or respiratory secretion (Fig. 1.3) (Centre for Disease Control and Prevention 2020c). Healthcare professionals are at the highest risk of getting SARS-CoV-2 infection from infected patients and therefore extreme precaution needs to be taken while handling COVID-19 patients. International travelers presenting any symptoms of SARS-CoV-2 should be isolated and quarantined to prevent further infections (Gostic et al. 2020). Apart from these personal protective measures, development of effective vaccine is the ultimate way of controlling SARS-CoV-2 infection. Using bioinformatics approaches, novel cytotoxic T lymphocyte (CTL) generated from spike glycoproteins may be used to develop effective vaccine for SARS-CoV-2. The first SARS-CoV-2 vaccine, namely, mRNA-1273, is under clinical trial and involves 45 volunteers who have received two intramuscular injections at an interval of 28 days (U.S. National Library of Medicine 2020).

1.7 Conclusions

SARS-CoV-2 has been declared a pandemic that causes COVID-19. Infected individuals have been reported with common flu-like symptoms and cytokine storm syndrome in severe cases. Diagnosis of COVID-19 relies on the detection of nucleic acid tests by RT-qPCR. Current treatment relies on the symptomatic relief of the patients. However, several repurposing drugs like favipiravir, remdesivir, chloroquine, and TMPRSS2 protease inhibitors have been shown to be effective. Personal protective measures should be followed to prevent SARS-CoV-2 infection. In addition, a clinical trial of SARS-CoV-2 vaccine, mRNA-1273, has been started.

1.8 Future Perspectives

The emergence of any infectious viral disease is difficult to anticipate, even though use of spatial epidemiology and mathematical modeling may predict the occurrence of emerging or re-emerging diseases like COVID-19. RNA recombination, mutation, and reassortment as well as other factors including globalization, expanding human population, deforestation, and altered ecosystems are the most convergent forces for the emergence of viral infectious diseases. SARS-CoV-2 infection is of global public health and economic importance and therefore needs collective government and societal response. Considering the escalating number of cases worldwide, the WHO has declared SARS-CoV-2 as a pandemic. The global shutdown of trade and travel may result in a reduction in the transmission rate of SARS-CoV-2. Personal protective measures should be implemented to reduce the risk of SARS-CoV-2. In order to prevent the spread of SARS-CoV-2 infection, several major steps should be taken, for instance strengthening surveillance and conducting awareness programs. In addition, extensive applied research should be funded and executed to understand the molecular mechanism and to develop effective prevention and control strategies for COVID-19.

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