REVIEW ARTICLE

Update on COVID-19 Pandemic

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Abstract

Objective: This update is concerned on the coronavirus disease (COVID-19) pandemic that is affecting the globe. The aim of this update is to summarize the up-to-date knowledge about the virus, its way of transmission, clinical features, diagnosis, and treatment.

Result: The COVID-19 is a public health threat affecting humankind currently after the emergence and spread of the novel coronavirus or the severe acute respiratory syndrome coronavirus 2. The virus is believed to have originated from bats and transmitted to humans. Around 1.5 million peoples are confirmed to have the COVID-19 and more than 83000 individuals have died of it by April 8, 2020, all over the world. It is transmitted by inhaling or having contact with droplets. The incubation period ranges from 2-14 days. It manifests mainly with fever, non-productive cough, and dyspnea. The polymerase chain reaction from various samples like throat swabs, nasal swabs, bronchoalveolar lavage fluid is used to confirm the diagnosis. High-resolution chest computerized tomography is abnormal in most patients, and typical findings are ground glass patchy opacities on both lungs and sub-segmental consolidation. Treatment is largely supportive. However, trials are ongoing, and chloroquine and hydroxychloroquine have got a lot of attention in the battle against COVID-19.

Keywords: COVID-19, RT-PCR, SARS-CoV-2, Treatment.

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Introduction

In December 2019, an outbreak of unusual pneumonia was reported in Wuhan, Hubei, China, with many cases linked to Huanan Seafood Market that sells seafood and live exotic animals. Two patients, who had fever, cough, and bilateral ground-glass opacities on both lungs with patchy infiltration were confirmed to have a novel coronavirus from the bronchoalveolar lavage sample. Both patients had reported independent contact history with this market.[1] Environmental samples (33 out of 585 samples) from the Huanan seafood mark*et al*so tested positive, implying that the virus had originated from the market.[2] It is noted that most epidemic is caused by viral cross-species transmission from animals to human.

Similar viral outbreaks, albeit in a smaller range, had occurred during 2002/3, where severe acute respiratory syndrome (SARS) affected 8422 persons with 916 deaths (case fatality rate of 11%)).[3] Likewise, in 2012, a coronavirus caused respiratory illness named Middle East respiratory syndrome (MERS) first reported in Saudi Arabia and has affected 2494 persons till November 2019 in 27 countries and had resulted in 858deaths. Both the SARS CoV and MERS-CoV have originated from bats and the intermediate hosts were palm civet cats and dromedary camels in SARS CoV and MERS-CoV respectively.[4-8]

The outbreak of COVID-19 is believed to be fueled by the migration of the Chinese for the Chinese New Year. The outbreak has spread to other parts of China and later to other countries.

Result

Virology

Coronaviruses are enveloped positive-sense Ribonucleic acid (RNA) viruses ranging in size from 60 nm to 140 nm in diameter with spike-like projections on its surface, giving it a crown-like appearance under the electron microscope; hence the name coronavirus.[9] Alignment of the full-length genome sequence of the COVID-19 virus and other available genomes of Betacoronavirus showed the closest relationship was with the bat SARS-like coronavirus strain BatCov RaTG13, identity 96%.[10]

SARS-CoV-2 is closely related to two bat-derived severe acute respiratory syndrome-like coronaviruses, bat-SL-CoVZC45, and bat-SL-CoVZXC21(11). Whole-genome sequencing analysis of 104 strains of the COVID-19 virus isolated from patients in different localities with symptom onset between the end of December 2019 and mid-February 2020 showed 99.9% homology, without significant mutation.[11]

The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 as that for SARS-CoV and mainly spreads through the respiratory tract.[4]

The SARS-CoV-2 is strange with one of the hardest protective outer shells among coronaviruses. This implies that the virus may be highly resilient in saliva or other body fluids and outside the body. Thus, an infected body is more likely to shed a higher number of viral particles since it is more resistant to antimicrobial enzymes in body fluids. The viral particles are more likely to stay active for long. These factors could partly explain the greater contagiousness of

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the SARS-CoV-2 as compared to its predecessors, SARS-CoV, and MERS-CoV.[12]

Transmission

The initial transmission is believed to be cross-species, from animal to human. The reservoir of SARS-CoV2 is a bat, as supported by phylogenetic analyses. However, the intermediate host that has transmitted the virus to humans is not identified for sure. Nevertheless, pangolins, snakes, and turtles might have acted as the potential intermediate hosts.[13] The main mechanism of transmission for the virus is either inhalation of droplets or direct contact with droplets. The majority of the transmission occurs from symptomatic persons. Nevertheless, the asymptomatic transmission has also a role in the spread of COVID-19.[14-18] The median duration of viral shedding was around three weeks in survivors, while the SARS-CoV-2 was detectable till death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days, implying longer isolation of cases for preventing the viral spread.[19]

Family cluster transmission via close and unprotected exposure directly to droplets or indirectly with fomites in the immediate environment is the main reason for SARS-CoV-2 transmission. Nosocomial transmission is possible; however, it is not a major contributor.[20,21]

Human milk is not believed to be a vehicle of COVID-19, and asymptomatic or mildly sick COVID-19 infected mother could breastfeed her newborn with the necessary precautions in place. However, if the mother is too sick for caring for the newborn, then freshly expressed breast milk should be given to the newborn.[22]

SARS-CoV-2 was also isolated from anal swabs of COVID-19 infected individuals, raising a suspicion of a possible feco oral transmission.[23–25]

Pathogenesis and Clinical Features

Pathogenesis

Both viral and host factors play a role in the occurrence and development of COVID 19. The viral factors include virus type, mutation, viral load, viral titer, and viability of the virus in vitro. The host factors include genetics, age, gender, nutritional status, neuroendocrine-immune regulation, and physical status. The interaction of these two factors will determine the occurrences of infection, the severity of the disease and the likelihood of recovery and death.[26]

Both humoral and cellular immunity will be activated and have a role in the manifestation and containment of COVID-19 infection. Virus-specific B and T lymphocytes mediate both humoral and cellular-based immunity. Like other acute viral infections, antibodies will be produced against SARS-CoV-2. Immunoglobulin M (IgM) and immunoglobulin G (IgG) will be apparent. IgM implies acute infection and is expected to disappear in 12 weeks after infection, while IgG will be long-lasting. It has to be determined if IgG is protective of re-infection.[26] The number of CD4+ and CD8+ T cells was found to be significantly reduced.[27]

Clinical Features

The incubation period of SARS-CoV2 ranged from 2-14 days, with a mean of 5.2 days.[28] The clinical spectrum of SARS-CoV-2 infection variable, comprising asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death.[19]

More than 200 countries are affected by the COVID-19 pandemic. Nearly 1.5 million people are infected with SARS-CoV-2, and among them, more than 83,000 have died (as of April 8, 2020). United States of America, Spain, and Italy are among those that are highly affected by COVID-19(29). The following graph depicts the epidemiology of COVID-19 in selected world countries.

All age groups are affected, including neonates and the elders.[30] It also affects pregnant women. There is no evidence of vertical transmission of SARS-CoV-2; however, an increased prevalence of preterm deliveries has been noted.[31,32]

The symptoms of COVID 19 include fever, non-productive cough, difficulty breathing, myalgia, and fatigue.[26,33,34] Less common symptoms of COVID-19 include sputum production, headache, hemoptysis, chest pain, muscle ache, rhinorrhea, nausea, vomiting and diarrhea.[35]

The major complications of COVID 19 are acute respiratory distress syndrome, acute cardiac injury, acute kidney injury, and shock.[35,36]

Pathology

Histological examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates. The lung showed evident desquamation of pneumocytes and hyaline membrane formation, indicating acute respiratory distress syndrome. Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, was seen in both lungs. Multinucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli were identified in the intra-alveolar spaces, showing viral cytopathic-like changes. No obvious intranuclear or intracytoplasmic viral inclusions were identified.[27]

Mortality and its Risk Factors

The time from the onset of COVID-19 symptoms till death ranged from 6 to 41 days, with a median of 14 days. The time from onset of symptom to death was shorter in those aged 70 years or older as compared to those younger than 70 years.[37] Older age, higher sequential organ failure (SOFA) score at admission, elevated d-dimer (> 1microgram/mL) were found to be associated with increased risk of in-hospital death.[19] One of the major reasons for death in COVID-19 is acute respiratory distress syndrome.[35,36]

Diagnosis

If a person has symptoms suggestive of COVID-19 such as fever and /or respiratory symptoms like non-productive cough and dyspnea and having a travel history to COVID-19 affected

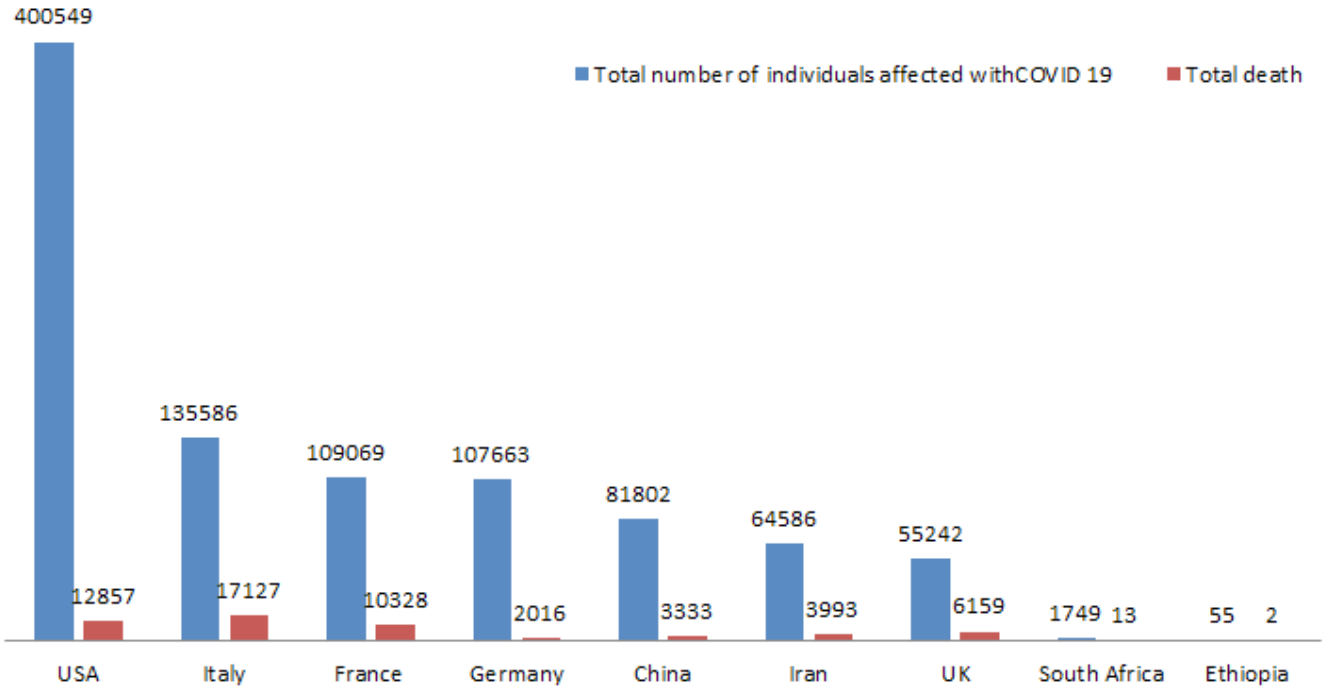

Figure 1: Summary of the COVID-19 epidemiology of selected countries, as of April 8, 2020

region or residing in COVID-19 affected area or having close contact with someone with respiratory symptoms, COVID-19 should be suspected. Necessary precautions should be practiced by those giving care to such individuals.

Among the investigations required to confirm the diagnosis of COVID-19 are real-time reverse transcription-polymerase chain reaction (RT-PCR) tests on throat swab, nasal swabs, bronchoalveolar lavage fluids, or blood samples. Currently, RT-PCR test remains the standard test to make a definitive diagnosis.[38] Other investigations that are required include complete blood count, which could be normal or could reveal decreased leukocyte count. Arterial blood gas analysis shall be done in those who have difficulty breathing. Liver and kidney function tests are other important tests.

Chest radiography could be normal in COVID-19 pneumonia; hence relying on it could be misleading.[39] However, in severe cases chest X-ray could reveal multiple patchy shadows in both lungs.

Chest computerized tomography is the main imaging technique used in the diagnosis of COVID-19. The most common finding is Ground-glass opacity that is mostly bilateral and multi-lobar. The other common finding is consolidation. Nevertheless, findings like discrete nodules, cavitations, pleural effusion, and lymphadenopathy were not observed in a study by Chung *et al*.[40]

Treatment

The majority of COVID-19 patients will be asymptomatic or have mild disease and will not require treatment or may need symptomatic treatment. However, for those with severe disease, different treatments will be required, including maintaining fluid balance, acid-base balance, administering oxygen, and using mechanical ventilation. Some of the specific management are discussed in the following paragraphs.

Immunosuppression could be protective of severe forms of COVID-19.[41] administration of lopinavir/ritonavir significantly decreased viral loads and no or little coronavirus titers were observed.[42] On the contrary, other studies showed no benefit from lopinavir/ ritonavir as compared to standard care severely sick COVID-19 patients.[43]

The other drugs that were used in COVID-19 patients are hydroxychloroquine and chloroquine.[44] Both drugs have resulted in decreased respiratory viral load after administration, though further studies are required in this regard. These drugs are primarily used in the treatment of rheumatologic diseases like rheumatoid arthritis and systemic lupus erythematosus. The widespread use of these drugs could result in a shortage of drugs for rheumatologic patients.[45,46] The addition of azithromycin to hydroxychloroquine was significantly more efficient for virus elimination.[46] Ongoing clinical trials are testing the efficacy of chloroquine.[47] More than twenty in vivo clinical trials are registered to test chloroquine and hydroxychloroquine for the treatment of COVID-19.[48,49]

Treatment of COVID-19 with inhalational interferon was not found effective, rather worsening was noticed.[50]

Hopeful drugs that may be helpful in the treatment of COVD-19 include Favipiravir.[51]

Traditional Chinese Medicines (TCM) has been used in different Chinese hospitals as an add-on therapy to other measures like antivirals; antibiotics and oxygen

supplementation was found to be effective. However, lack of control groups, absence of randomization, blinding, and allocation of concealment are concerns about the actual benefits of TCM. Additionally, the lack of clear evaluation indicators and the absence of long-term efficacy and follow-up could be setbacks in taking the available pieces of evidence for granted for using TCMs.[34]

Prevention

Entry screening for H1N1 Influenza during 2009 using a Thermal scanner at the airport had low sensitivity (only 5.8 %).[52] Border screening with various techniques like self-identification, thermal scanning, and/or visual inspection is resource-intensive. It could also consume public health personnel needed for other essential activities. However, it could be beneficial in creating awareness about the outbreak and/or pandemic among travelers.[53] Thermal screening alone for the prevention of COVID-19 is not very important because of the potential transmission by asymptomatic individuals as well.[54]

Affected countries are using different mechanisms of preventing and containing COVID-19 spread depending on their risk. Among the mechanisms used contacts tracing, self-isolation or quarantine, promotion of public health measures, including handwashing, wearing personal protective equipment like facemasks, and social distancing. Postponing or canceling less important gatherings or handling it with video-conferencing or webinar is essential. Special emphasis and measures to protect or diminish transmission should be given to susceptible populations, including children, health care providers, and older adults.[55]

Limitation(s)

The COVID-19 pandemic is an emerging infection, and knowledge is evolving. Thus the knowledge included in this update could be changed shortly as more studies are done and made available.

Declarations

Ethics approval and consent to participate

- Not applicable

Consent for publication

- 'Not applicable.'

Availability of data and materials

- All important data are included in the manuscript

Competing interests

- Author declares no competing interest

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