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COVID-19 Pandemic

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الاهداء

إلى من أُفضِّلها على نفسي، ولِمَ لا؛ فلقد ضحَّت من أجلي

ولم تدَّخر جُهدًا في سبيل إسعادي على الدَّوام

(أُمِّي الحبيبة).

نسير في دروب الحياة، ويبقى من يُسيطر على أذهاننا في كل مسلك نسلكه

صاحب الوجه الطيب، والأفعال الحسنة.

فلم يبخل عليَّ طيلة حياته

(والدي العزيز).

إلى أصدقائي، وجميع من وقفوا بجواري وساعدوني بكل ما يملكون، وفي أصعدة كثيرة

أُقدِّم لكم هذا البحث، وأتمنَّى أن يحوز على رضاكم.

الشكر والتقدير

أول مشكور هو الله عز وجل، ثم والداي على كل مجهوداتهم منذ ولادتي إلى هذه اللحظات، أنتم كل شيء أحبكم في الله أشد الحب.

يسرني أن أوجه شكري لكل من نصحني أو أرشدني أو وجهني أو ساهم معي في إعداد هذا البحث بإيصالي للمراجع والمصادر المطلوبة في أي مرحلة من مراحله، وأشكر على وجه الخصوص استاذي الفاضل الدكتور (إسماعيل إبراهيم لطيف) على مساندتي وإرشادي بالنصح والتصحيح وعلى اختيار العنوان والموضوع، و أتوجه بالشكر و التقدير الى كادر و تدريسيي كلية الطب بجامعة ديالى لجهودهم المثمرة في تسهيل المهمة الدراسية للطلاب في ظل الظروف الصعبة الراهنة راجيا من الله عز وجل التوفيق و السداد للجميع...

Abstract

Corona virus disease (COVID-19) is one of the Coronaviradae that cause a sever viral Pneumonia. In December 2019, China anounced the first 4 cases of the disease in Wuhan, and it outbroke rapidly until the WHO announced the disease as a "Pandemic" in February 2020. By fourth of April 2021, the incidence exceeded 131 million case globally in more than 190 countries . It is a worldwide problem that gave a destructive hit to both health authorities and governments around the world. It's main manifestation include severe dyspnea , cough, chest pain and high grade fever. There is no definite clinical or laboratory test that can diagnose the infection 100%. So, the diagnosis is made on basis of a mix of clinical finding, laboratory finding and CT findings. No curable treatment is available currently for the infection and all world treatment protocols is mainly symptomatic and supportive. the recent announcements about the new Vaccines by Pfizer and ASTRA/zeneca companies after getting the American food and drug agency (FDA), seem to be promising and rising hopes to eradicate the infection by the end of 2022.

Keywords: COVID-19 , Pandemic, vaccine

Introduction

In December 2019, a clustering pneumonia of unknown etiology occurred in Wuhan, Hubei Province, China. The emerging disease has spread rapidly from Wuhan to other parts of China and to other countries. Through a deep sequencing analysis, International Committee of Taxonomy of Viruses (ICTV) has designated the virus responsible for this epidemic pneumonia as SARS-CoV-2 [(1)].

Coronavirus is one of the major pathogens that primarily targets the human respiratory system. Previous outbreaks of coronaviruses (CoVs)

include the severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV which have been previously characterized as agents that are a great public health threat. [(2)] The pandemic of coronavirus disease 2019 (COVID-19) is spreading rapidly. Although the cause was quickly identified as a new coronavirus named SARS-CoV-2, our knowledge of this novel virus remains very limited. High infectivity of the virus, lack of effective antivirals and vaccines, and potentially large asymptomatic populations, have made management of COVID-19 extremely challenging. [(3)]

The World Health Organization (WHO) has recently declared coronavirus disease 2019 (Covid-19) a public health emergency of international concern.9 As of February 25, 2020, a total of 81,109 laboratory-confirmed cases had been documented globally.[(4)] The pandemic of COVID-19 is not only a health issue; it is also a financial burden on citizens, health-care providers, and the governments. GDP (Gross domestic product) dropped by $1.73 trillion (an annualized rate of 31.7 percent) from the first to the second quarter of 2020, according to the Bureau of Economic Analysis (2020). During the isolation, GDP dropped largely due to a decline in personal consumption expenses and the closing of most economic institutes.[(5)] From this short article , we will demonstrate the microbiology, transmission, clinical features , management and the prognosis of COVID-19.

Virology

Coronavirus particles consist of a ;30-kb strand of positivesense RNA that forms the genome; this genome is coated with nucleocapsid (N) protein and enclosed in a lipid bilayer containing three membrane proteins: spike (S), membrane (M), and envelope (E).[(6)] For all known coronaviruses, the M protein is critical for incorporating essential viral

components into new virions during morphogenesis, and N protein associates with the viral genome and M to direct genome packaging into new viral particles.[7] The E protein forms an ion channel in the viral membrane and participates in viral assembly. The S protein is required for viral entry, as it binds to the target cell and initiates fusion with the host cell membrane. [8]

Port of entry

S is homotrimeric, with each subunit consisting of two domains, S1 and S2. S1 contains the receptor-binding domain (RBD) and engages with the host receptor, whereas S2 mediates subsequent membrane fusion to enable the virus to enter the host cytoplasm.[9] The first cleavage site is at the S1/S2 boundary, leading to structural changes in the S2 domain that place it in a prefusion conformation. This cleavage event also separates S2 from S1. The second cleavage site is at S2, which drives fusion of the viral and cellular membranes to enable release of the N-coated RNA genome into the cytoplasm. [7, 9]

The S proteins of both SARS-CoV and SARS-CoV-2 use host ACE2 as their receptor. ACE2 is a cell-surface peptidase that hydrolyzes angiotensin II and is expressed in most organs, with particularly high expression in the epithelia of lung and small intestine.[10] Numerous therapeutic strategies are being explored to inhibit SARS-CoV-2 entry, including blocking ACE2 engagement, inactivating host proteases, and inhibiting S2-mediated membrane fusion. Neutralizing antibodies against SARS-CoV S display moderate efficacy in blocking SARS-CoV-2 infection due to significant differences in the epitope region. [11]

Viral replication

Coronaviruses have one of the largest known genomes among RNA viruses, ranging from 27 to 32 kb in length, more than double the length of the average RNA virus genome, and encode for 22-29 proteins.[12] A subset of nsps generated by proteolytic cleavage of the polyproteins come together to form the replication and transcription complexes (RTCs) that copy and transcribe the genome. RTCs reside in convoluted membrane structures derived from rough endoplasmic reticulum (ER) and are anchored in place by viral transmembrane proteins nsp3, nsp4, and nsp6.[13]

The replication of coronaviruses involves synthesis of the complementary full-length negative-strand RNA, which serves as a template for generation of positive-strand progeny genomes. In addition, the RTCs also carry out synthesis of subgenomic (sg RNA) mRNAs, which encode for the ORFs located in the 39-proximal one-third of the genome. Regulation of the levels of some sg mRNAs, such as the N protein sg mRNA in coronaviruses, was shown to be mediated by short- and long range RNA-RNA interactions.[14]

Assembly and budding

The assembly of an infectious CoV virion requires that its nucleocapsid, consisting of the viral RNA genome coated with N protein, and viral envelope coalesce into the same intracellular space. Viral glycoproteins that are incorporated into the envelope (M, E, and S proteins) are translated in the ER and retained at the site of budding in the ERGIC (endoplasmic-reticulum–Golgi intermediate compartment).[15] The ERGIC budding site is distinct from the site of viral genome synthesis in the RTC. The nucleocapsid core of the virion traffics from the RTC to ultimately bud

into ERGIC membranes, which are decorated with M, E, and S protein and become the lipid envelope of the virion.[16]

Pathogenesis

SARS-CoV-2 binds to ACE 2, (Angiotensin converting enzyme receptors type 2), the host target cell receptor. Active replication and release of the virus in the lung cells lead to non-specific symptoms such as fever, myalgia, headache, and respiratory symptoms.[17] The distribution of ACE 2 receptors in different tissues may explain the sites of infection and patient symptoms. For example, the ACE 2 receptor is found on the epithelium of other organs such as the intestine and endothelial cells in the kidney and blood vessels, which may explain gastrointestinal symptoms and cardiovascular complications.[18]

Lymphocytic endotheliitis has been observed in postmortem pathology examination of the lung, heart, kidney, and liver as well as liver cell necrosis and myocardial infarction in patients who died of COVID-19. These findings indicate that the virus directly affects many organs, as was seen in SARS-CoV-1 and influenza.[19] The complete pathogenesis is remain not well understood and need more time and study.

Mode of transmission

The primary mode of transmission of SARS-CoV-2, like other coronaviruses, is through infected respiratory droplets, with viral infection occurring through direct or indirect contact with nasal, conjunctival, or oral mucosa when respiratory particles are inhaled or deposited on these mucous membranes.[20] Close range communication (such as 15 minutes face to face and within 2 m) accounts for the majority of transmission, and spread is particularly efficient within households and among family and friends. Infection risk is increased by sleeping in the same room as, or being

married to, an infected person, but infection risk is reduced by isolating the infected person from the rest of the family.[21]

The role of faecal shedding in SARS-CoV-2 transmission and the extent of fomite is well established recently. Both SARS-CoV-2 and SARS-CoV-1 remain viable for many days on smooth surfaces (stainless steel, plastic, glass) and at lower temperature and humidity (eg, air conditioned environments).Thus, transferring infection from contaminated surfaces to the mucosa of eyes, nose, and mouth via unwashed hands is a possible route of transmission.[18]

Clinical features

The typical respiratory symptoms include shortness of breath, fever, usually dry cough but may be productive, chest pain, sore throat, tiredness and anosmia. The non-respiratory symptoms include diarrhea, loss of appetite, loss of taste sense , neurological symptoms such as , headache , dizziness , altered mental status , Guillian- barre syndrome and rarely stroke.[22,23] Cardiovascular events not common, but, have been associated with covid-19 include myocardial injury, especially in patients with severe infections, because the infection associated with hypercoagulable state, myocarditis and myopericarditis with reduced systolic function , cardiac arrhythmias and heart failure.[23] Ocular symptoms include conjunctivitis, congestion and hyperemia also reported. On physical examination, the patient may look ill, pale, tachypneic, wheezing in the stethoscope with or without crepitations.

Diagnosis

The laboratory investigation after admission show leukopenia and increase in inflammatory marker such as CRP. Real time polymerase chain reaction (RT-PCR), is a diagnostic test that uses nasal swab, tracheal

aspirate or bronchoalveolar lavage (BAL) specimens. The primary, and preferred, method for diagnosis is the collection of upper respiratory samples via nasopharyngeal and oropharyngeal swabs. The use of bronchoscopy as a diagnostic method for COVID-19 is not recommended as the aerosol that is generated poses a substantial risk for both patients and healthcare staff.[24]

Typical CT findings in individuals with COVID-19 were ground-glass opacities, particularly on the peripheral and lower lobes, and bilateral multiple lobular and subsegmental areas of consolidation, especially in ICU patients.[25]

Non-typical CT findings included pleural effusion (only about 5%), masses, cavitations and lymphadenopathies; therefore, these would suggest alternative diagnoses. Conventional chest X-ray sensitivity is lower at around 59%. Ultrasound has been used as a diagnostic tool in a very limited number of cases (due to decrease sensitivity and patient factors that affect the results).[25]

Management

It is fundamental to ensure patient isolation in order to avoid transmission to other patients, family members and healthcare providers. Quarantine measures must be taken to isolate infected individuals, both symptomatic and asymptomatic, and anyone who may have been in contact with them. There is no authorized drug can treat the infection. Several research from previous Corona pandemics showed that certain antiviral drugs (Remdesivir, Lopinavir) were effective in preventing viral replication and infection.[26]

The WHO recommend the usage of systemic corticosteroids rather than no systemic corticosteroids for the treatment of patients with severe

and critical COVID-19 (strong recommendation, based on moderate certainty evidence). However, no recommendation for mild infection.[27]

Oxygen therapy will be required if hypoxia is present (SatO2 < 93%) or if symptoms of respiratory distress become evident. Oxygen therapy is generally administered through a (high-flow) nasal cannula, a facemask or noninvasive ventilation. The use of toscilizumab needs to be rationalised. Its short-term (one to three doses) use is not free from serious adverse events, and a vigilant monitoring is mandatory.[28]

Anticoagulation therapy is recommended in patients with early-stage COVID-19, especially when the D-dimer value is 4 times higher than normal (26). The prognosis is good with more the 97% cure and 3% mortality.

Prophylaxis

Simple successful prophylactic steps include wearing a mask, wearing medical gloves, and using a local disinfectant. Incidence rates in the population are minimized by quarantine and isolation. Vaccine experiments conducted recently appear to be successful. Following the FDA's approval of Pfizer's vaccine, all health agencies across the world are rushing to purchase and use the latest vaccines in the hopes of eradicating the pandemic by 2022.

Complications

The kidneys are one of the most frequently affected extrapulmonary organs in patients infected with SARS-CoV-2; especially, in those patients who are severely ill. Currently, the occurrence of acute kidney injury (AKI) among patients with COVID-19 is not consistent across published studies, ranging from 0.1% to 29%.[27] Olfactory and gustatory dysfunction occur

in 30-50% of the patients. Cardiac events and arrhythmias also reported. Some studies shows elevation in Liver enzymes (AST, Billirubin, LDH and PT) in severely ill patients which indicate liver injury. Hematopoetic problems such as leukopenia and lymphopenia are not uncommon. Septic shock and DIC are quite rare complications but a serious cause of mortality.[27]

Conclusion

COVID-19 is mainly respiratory disease that outbreaks and became a pandemic in the last 18 months. No specific drugs can cure the disease but there is a hope in the new vaccine to eliminate the global pandemic.

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