Tanveer A Khan et al; An Insight on Coronavirus



Coronavirus- A Cause of Current Pandemic

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Abstract

SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus-2) is RNA virus and is the cause of current pandemic. It was 1st detected in a patient in December 2019 in China. It is mainly responsible for respiratory illness which can progress to acute respiratory distress syndrome (ARDS) and even can be responsible for death. They are largest, enveloped, single-stranded, positive-sense RNA viruses. In the present review, we have tried to summarize the various aspects of Covid-19 including properties, pathological features, clinical presentation and management strategies.

Keywords: Coronavirus, Covid-19, RNA dependent RNA polymerase

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Introduction

SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus-2) a novel RNA coronavirus is the cause of current pandemic. Coronavirus were known to cause common cold in humans till the 2002 but in 2002 SARS-CoV and in 2013 MERS-CoV (Middle East Respiratory Syndrome Corona Virus) emerged. In December 2019 in Wuhan, Hubei province of China SARS-CoV-2 was identified. SARS-CoV and MERS-CoV were highly pathogenic to human being and caused severe respiratory syndrome. ^{1,2,3} SARS-CoV, MERS-CoV and SARAS-CoV-2 are more dangerous as they have the ability to severely affect lower respiratory tract and can cause acute respiratory distress syndrome (ARDS) leading to even death.

Human coronaviruses is mainly responsible for respiratory and enteric infection. ^{4,5} The presenting symptoms are mainly flu-like symptoms such as fever, cough and asthenia which are similar to other coronaviruses. Severe lung injury is observed in many cases in all age groups and specifically in individuals with high risks such as elderly persons, persons associated with comorbid conditions like diabetes and cardiovascular conditions. Patients of Covid-19 typically shows dyspnoea and radiological signs among other clinical features. The condition progress to severe interstitial pneumonia, acute respiratory distress syndrome and ultimately progress to multiorgan failure and responsible for even death. ⁶ In the present review, we have tried to summarize the various aspects of Covid-19 including properties, pathological features, clinical presentation and management strategies.

History

1st case of SARAS-CoV-2 (Covid-19) was detected in a 41-year-old man who was admitted to the Central Hospital of Wuhan on 26 December 2019. The Wuhan Centre for Disease Control and Prevention after epidemiological study found that the person was working in a

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local indoor seafood market where, a number of wild animal were available for sale including birds and snakes. ⁷ After that (Covid-19), the cause of current pandemic caused 216,025 deaths till mid-October 2020 in the United States and more than one million documented deaths within the early October world-wide. ^{8,9} The World Health Organization (WHO) named the disease as coronavirus disease 2019 (Covid-19) and declared it pandemic due to its high infectivity rate and high contagion rate.



Figure 1. Structure of SARAS-CoV-2

Coronavirus properties

Coronaviruses are a group of enveloped RNA viruses. They are largest, enveloped, singlestranded, positive-sense RNA viruses. The order of corona virus is Nidovirales and family Coronaviridae and subfamily Orthocoronavirinae. They contain four genera, namely Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and *Deltacoronavirus*. SARAS-CoV-2 belongs to genus Betacoronavirus.

Coronaviruses have positive sense, singlestranded RNA genome and a nucleocapsid of helical symmetry. They have club-shaped spikes which project from their surface. Coronavirus measures around an average of 30 kilobases. Apart from RNA, there are four essential structural proteins namely spike (S) glycoprotein, envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein ^{10,11}



Figure 2. Coronavirus Taxonomy

Epidemiology

The outbreak of SARS-CoV-2 is associated with Wuhan Huanan seafood market with wild animals but the specific animals which were the cause of Covid-19 were not identified. According to WHO, the environmental samples which were taken from the Huanan seafood market tested positive for SARS-CoV-2. ¹² The expected animal host for SARS-CoV-2 is Bats as bats are the host for more than 30 coronaviruses and previous evidences also favours this. ¹³ As far as intermediate host is concerned, the most probable animal is

pangolin for the SARS-CoV-2 although it may not be the only animal as intermediate host. ¹⁴

Huang C et al. ¹⁵ Chen N et al. ¹⁶ and Xu XW et al. ¹⁷ reported range of median age of patients between 41 to 57 years. Huang C et al. Chen N et al. also found male predominance (50-75%). There is a strong relationship between one or more underlying diseases such as hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease, and malignancy with SARS-CoV-2 infection as 25-50% cases of SARS-CoV-2 were observed among such patients. ^{15,16,18} The median incubation period of

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SARS-CoV-2 is between 3 to 24 days. Route of transmission in human is via droplets from coughing or sneezing or direct contact. ¹⁹

Pathology

The susceptible host cell for viral tropism in case of SARAS-CoV-2 is Angiotensin Converting Enzyme 2 (ACE2) which is found in various part of human body including lungs, small intestine, kidneys, heart, thyroid and adipose tissue leading to variety of symptoms. ACE2 play role as functional receptor for SARS-CoV-2 which mediate viral entry into the host cell. ²⁰ SARAS-CoV-2 infect the ACE2 by their envelope spike glycoprotein (S-Protein), it is responsible for the entry of SARAS-CoV-2 into the host cell. In the 1st stage of viral infection, cleavage of S-protein occurs by which S1 and S2 proteins are formed. S1 is responsible for recognizing and binding with the cell surface receptor (ACE2) because of presence of receptor binding domain in it while S2 subunit contains other elements needed for the membrane fusion. The ectodomain S1 binds to

the peptidase domain of ACE2. As far as S2 protein is concerned, it's further cleavage occurs by the host cell serine protease which results in membrane fusion process. These two steps are responsible for viral entry into the ACE2 enzyme.²¹

Once the membrane fusion process over then the viral genome RNA is released into the host cell cytoplasm. The uncoated RNA translates two polyproteins, pp1a and pp1ab. These proteins encode non-structural proteins and they forms replication-transcription complex. The replication-transcription complex replicate and synthesize a set of subgenomic RNAs, which encode accessory proteins and structural proteins. The replication-transcription complex is also involved in genomic RNA. Thus newly formed genomic RNA, nucleocapsid proteins and envelope glycoproteins assemble and form viral particle buds. Once the translation and replication process over the virion-containing vesicles fuse with the plasma membrane and the new virions are then released by the process of exocytosis. 22,23,24



Figure 3. Coronavirus cycle

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Clinical Features

SARS-CoV-2 patients present a wide variety of clinical manifestations ranging from mild nonspecific symptoms to severe pneumonia with organ damage. Common symptoms are fever, cough, fatigue, dyspnea, myalgia, sputum production and headache. Less common symptoms are sore throat, rhinorrhea, chest pain, hemoptysis, conjunctival congestion, diarrhea, nausea, and vomiting. Sometimes patients may not have fever at the time of onset, it may develop after hospitalization of the patient. In few severe cases even fever was not observed at al.¹⁹

Laboratory findings

SARS-CoV-2, In lymphopenia, thrombocytopenia, and leukopenia are seen. Elevated levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum ferritin, and interleukin-6 (IL6) are observed. levels of d-dimer. Increased lactate dehydrogenase (LDH), creatine kinase (CK), prolonged prothrombin time. alanine aminotransferase (ALT), and aspartate aminotransferase (AST) also seen. 15,16,19

In chest computed tomography (CT), groundglass opacity, bilateral patchy shadows, and subsegmental areas of consolidation, sometimes with a rounded morphology and a peripheral lung distribution are visible. Apart from this a normal chest CT image is also observed in some cases. ^{15,16,19,24}

In lung biopsy specimens, bilateral diffuse alveolar damage with cellular fibromyxoid exudates are visible indicating pulmonary edema. Reduced and hyperactivated status of CD4 and CD8 T cells are observed in peripheral blood in SARS-CoV-2 cases. Pulmonary fibrosis is also markedly seen in these cases. ^{19,25} Diagnosis of SARS-CoV-2 is made on the basis of a positive result of real-time reversetranscriptase polymerase-chain-reaction (RT-PCR) assay. CT chest is the another diagnostic method. ^{19,26,27}

Management

Management strategies for COVID-19 include antiviral treatment, empirical antibiotic treatment, corticosteroid, intravenous immunoglobulin therapy and oxygen support. As of now there is no approved drugs for antiviral therapy against SARS-CoV-2. Among the antiviral drugs frequently used are Remdesivir, Oseltamivir, Ganciclovir, Lopinavir and Ritonavir. ¹⁹ In severe cases, role of corticosteroids are very important as they prevent acute respiratory distress syndrome. ²⁵

Conclusion

SARS-CoV-2 is novel RNA virus. It is largest, enveloped, single-stranded, positive-sense RNA virus. It is mainly responsible for respiratory illness, which can progress to acute respiratory distress syndrome. High-risk individuals including elderly patients and patients with comorbidity are at greater risk. Angiotensin Converting Enzyme 2 (ACE2) play role as functional receptor for SARS-CoV-2 which mediate viral entry into the host cell. Common clinical features are fever, cough, fatigue, dyspnea, myalgia, sputum production and headache. As of now, there is no specific antiviral agents available for the management of the Covid-19 although Remdesivir is promising drug, which has better effect than placebo and other antiviral agents. To relive Covid-19 related symptoms, patient must receive supportive therapy.

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