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CORONA VIRUS DISEASE (COVID 19) – AN INSIGHT ON THE ORIGIN, TRANSMISSION, PATHOLOGY AND THERAPIES

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ABSTRACT

In late 2019, a new human corona virus was reported in the city of Wuhan, Hubei Province, China, which was considered as the causative agent for the severe acute respiratory syndrome, which was later proclaimed by World Health Organization as a Public Health Emergency. It is important to know and update on the knowledge about the physical and behavior of the novel corona virus (SARS-CoV-2) such that it can help to improve the measures taken to control the pandemic. The main objective of this present work is to compile the various insights about the novel corona virus (SARS-CoV-2) in terms of its pandemic spreadability and mortality.

Keywords: COVID 19, nCoV-2019, Pandemic, Corona virus, SARS-CoV-2

INTRODUCTION

In the late 2019, the health authority of China reported the World Health Organization (WHO) about a spread of pneumonia with a much different etiology in Wuhan, Huebei. In the early January 2020, the cause of this epidemic was identified from a patient's swab as an infection caused by a novel corona virus originally abbreviated by WHO as 2019-nCoV **[1]**. Later, the pathogen was renamed as Severe Acute Respiratory

Syndrome Corona Virus 2 (SARS-CoV-2) and the ailment was designated as corona virus disease 2019 (COVID-19) by WHO **[2]**.

The Chinese Center for Disease Control and Prevention (CCDC) established a novel 2019-nCoV β corona virus, now officially known as Corona virus 2 (SARS-CoV-2) severe acute respiratory syndrome **[3]**. Since the onset of the 21st century, this is the third outbreak of the corona virus from the zoonotic origin, which raised drastic health concerns at the global level. During March 2020, the World Health Organization (WHO) raised major concerns over the rapid and uncontrolled spread of the epidemic, the failure of the actions taken by some countries in controlling the spread of the disease etc. Due to the unprecedented spread of the disease across the world, the WHO has declared that COVID-19 should be considered as a pandemic **[4]**. Since the outbreak of the pandemic, the reports and literature that are available till date are enormous. Hence, the main intent of this current review is to compile the day to day understanding of COVID-19 including the viral morphology, pathogenesis, diagnostic methods, and currently available therapeutic agents, strategic plans to control and prevent the pandemic.

Virology and Origin

Novel Corona virus belongs to the orthocoronavirinae, subfamily from the Nidovirales family, which are believed to be the primary causative agent for various respiratory and gastrointestinal tract infections. Coronavirinae and Torovirinae are the two important subfamilies; notably, the Coronavirinae subfamily is further divided into four major genus namely (A). Alpha corona virus that contains Human Corona Virus ((HCoV)-229E and HCoV-NL63) (B). In Beta corona virus - HCoV-OC43, Severe Acute Respiratory Syndrome human coronavirus (SARS-HCoV), HCoV-HKU1, and Middle Eastern respiratory syndrome corona virus (MERS-CoV): (C). Gamma corona virus- comprises of viruses of birds and whales (D). Delta corona virus- includes viruses that were isolated from pigs and birds **[5]**. Among the different corona viruses, HCoV-229E and HCoV-NL63 (α-CoVs) and β-CoVs HCoV-HKU1 and HCoV-OC43 (β-CoVs) were reported to have caused minimal symptoms and pathogenicity in the respiratory system. On the other hand, other β-CoVs like SARS-CoV and MERS-CoV were shown to have caused very serious infections, which were found to be fatal for the mankind **[6, 7]**.

The evolution of the epidemic like SARS and MERS from bats through a zoonotic origin. Interestingly the genomic comparison of SARS and SARS-CoV-2 viruses showed that about 380 amino acid substitutions had occurred among the SARS and SARS-CoV-2 like corona viruses. Notably, the changes were primarily focused on the non-structural protein genes. On the other hand, about 27 mutations were observed in the genes that were responsible for coding the viral spike proteins, which are in turn responsible for the receptor binding and cell entry in the host cell. From the available reports, it was observed that novel SARS-CoV-2 is a pathogen that showed preference for the human host cells. Structurally the pathogen consists of positive-sense single-stranded RNA (+ssRNA) enveloped and surrounded by S spike proteins **[8-10]**. The plausible mode of human mediation is the capability of the virus to bind with the host human cells. The reports also suggests that the COVID-19 also shares the same the angiotensin-converting enzyme 2 (ACE2) similar to that of the SARS-CoV **[11]**. It was also shown from the earlier reports that the onset of viral attachment depends on the binding efficacy between the human ACE2 receptor and viral receptor binding domain (RBD), which in turn determines the host susceptibility to SARS-CoV-2. More interestingly, the affinity shown by the S protein of COVID-19 and ACE2 is remarkably higher than the binding affinity exhibited by others. The different viral factors in turn could attribute to the rapid evolution of the virus and the transmission among the humans at a pandemic level (**Figure 1**).

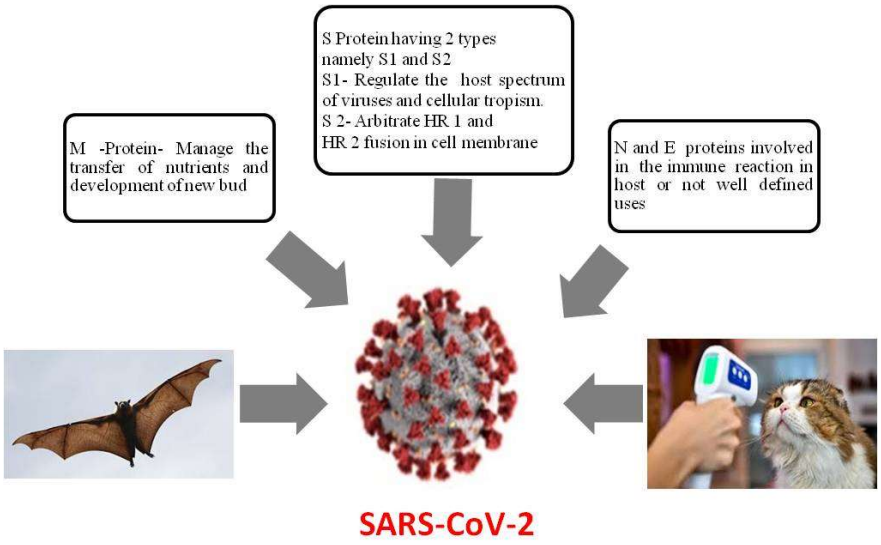

Figure 1: Different viral factors contributing for SARS-CoV-2

Epidemiology- Reservoirs and Treatment

It was reported that this viral infection had possibly originated from the wholesale seafood market in Wuhan, Central China and the reports showed that the virus would have got transmitted from Bats, **[12, 13]**. Based on the genetic information of the novel corona virus, it was named as SARS-CoV-2 as it shared the sequence similarity with SARS CoV **[14]**. The latest epidemiological data of COVID-19 virus are presented in **Table 1**.

Table 1: Epidemiology characteristics of COVID 19*

S. No.	Contents	COVID-19
1	Origin	Wuhan, China
2.	Total cases	44,67,21,660
3.	Recovered	37,98,69,780
4.	Total Death	60,20,582
5.	No. of Countries affected	226
6.	Health Care workers (%)	3.8
7.	Reproductive number	5.7
8.	Incubation period (days)	4.75-6.24
9.	Common symptoms	Fever, dry cough, dyspnoea, chest pain, loss of taste and smell, fatigue and myalgia
10.	Rare symptoms	Headache, abdominal pain, nausea, vomittng, diarrhoea

* as on 7th March 2022 (www.worldometers.info/coronavirus/)

The reason for assumption that the possible reservoir for COVID-19 virus could be bats because the genomic array of the virus isolated from the bat (Bat CoV RaTG13) showed about 96.2% similarity with that of COVID-19 virus **[15, 16]**. In addition, the analysis of the protein sequences and phylogenetic protocols have confirmed the presence of identical receptor residues in animals other than bats **[17]**. This provides additional options of considering other animal models like turtles, pangoline and snakes as alternative hosts reservoirs.

It was observed from the mode of human transmission is that the spread of SARS-CoV-2 occurs mainly among family people and friends where one has a close contact with the infected person or the asymptomatic carriers. It was reported that the early spread of the pandemic had occurred in .about 32% of infected individuals who had visited the Wuhan city and 72% of the outsiders of Wuhan city had developed the infection due to the close contacts with the people who were staying in the city **[18]**. The mode of transmission among humans is mainly due to the respiratory droplets that come from the infected person in the form of sneeze or cough. Nevertheless, the transmission of the COVID-19 in an asymptomatic manner still remains controversial and a recent report also claimed that the disease spreads in an asymptomatic manner as well **[19]**. However, one cannot rule out the possibility of body fluid interaction or fomite transmission.

Another important parameter in epidemiology is the basic reproduction number (R_0), which indicates the spread of the virus among the population. This value is not a biological constant for a particular pathogen and is likely to give an idea about the possible numbers of new infection that is caused from an infected person. Thus, the reproductive number is revised periodically along with the outbreak pattern and the interventions. The reproductive number for 2019-nCoV was reported as 2.24–3.58 **[20]** and is currently updated as 5.7. This value could have been calculated based on various analytical methods and validating the underlying assumptions.

Another interesting parameter in the pandemic is the incubation period, which states the time period between the initial exposure to an infectious agent to the appearance of signs and symptoms. A long duration of incubation can lead to highly asymptomatic and different subclinical infection levels. At the onset of the pandemic, about 425 cases were reported in Wuhan, which predicted the average period of incubation as 5.2 days (4.1-7.0 days) and later it was modified as 4.75 days (interquartile range: 3.0–7.2 days) **[21]**. Notably, the duration of incubation for COVID-19 virus is remarkably longer than SARS-CoV (4.0 days) and MERS-CoV (range 4.5-5.2 days)

Clinical Manifestations

A lot of clinical conditions were linked with SARS-CoV-2 infection; ranging from initial discomfort to mortality, which arises due to septicemia or acute respiratory distress syndrome (ARDS). The most common symptoms of COVID-19 infection includes fever, dry cough, shortness of breath, chest pain or pressure tiredness associated with myalgia. Other symptoms like headache, abdominal pain, nausea, vomiting, sore throat, conjuctivitis, diarrhoea, dizziness were moderately reported **[22]**. Infected individuals with ARDS and sepsis with abnormal hypotension although progressed rapidly but eventually resulted in multiple organ failure. Earlier reports showed that females were less prone to COVID-19 infection compared to the male population due to the role of X chromosomes and additional innate and adaptive immune system **[23, 24]**. It was also observed that co-morbidities like diabetes, hypertension and cardiovascular diseases enhanced the susceptibility of COVID-19 infection **[25]** and few other patients had shown noticeable upper respiratory tract infections and gastrointestinal disturbances **[26]**.

Diagnosis

The Central Government and the State Governments have taken tremendous efforts to monitor and control the transmission of COVID-19. As per the guidelines of WHO (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications), the Government recognized the use of real-time reverse transcription-polymerase chain reaction or RT-PCR as the '**gold standard**' to diagnose and confirm the COVID-19 infection.

Laboratory Investigations

The patients diagnosed with COVID-19 infection have shown common laboratory abnormalities such as decrease in lymphocyte counts **[27, 28]**, increase in prothrombin time, enhanced levels of lactate dehydrogenase (LDH), aspartate aminotransferase, creatine kinase, creatinine and C-reactive proteins **[29, 30]**. Few patients with severe bacterial sepsis and septic shock have shown increased procalcitonin levels. Critically ill COVID-19 patients had shown very high concentrations of proinflammatory cytokine such as IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A and TNFα in their plasma levels in comparison with the patients with mild to moderate symptoms **[27]**.

Radiology Investigations

Different factors like age, progression of the disease, immunity level, comorbidity and initial medical intervention has a direct impact on the radiological investigations **[31]**. Abnormal interventions like pneumonia were observed in the CT-scan of chest region. There were reports of multifocal ground-glass opacity; especially in the regions adjoining the peripheral parts of the lungs, occurrence of bilateral pulmonary parenchymal ground-glass consolidation or 'crazy paving' lesions in the pulmonary region mostly in the rounded form with a peripheral distribution were observed. In certain patients, respiratory swabs showed negative results, while their CT scan report strongly insisted the presence of the virus. The same patients were quarantined and tested positive for COVID-19 using RT-PCR diagnosis after 2-8 days **[30]**.

Risk factors

The prevalence of COVID-19 virus is commonly observed male adult population of the age group 34-59 years; patients with various comorbidities like cardiovascular, cerebrovascular diseases and diabetes are more prone to be infected with SARS-CoV-2. Extreme expression of the virus may also be linked to bacterial and fungal co-infection. There were fewer numbers of COVID-19

positive cases that were recorded among children under the age of 15 years and showed moderate clinical symptoms without any fever or pneumonia **[24]**.

Pathology investigation

Studies involving autopsy or histopathological investigations were often be the vital factor in understanding the structural features of the virus. Histopathological analysis of some patients showed edema, exudate of the protein, pneumocytic hyperplasia with limited patchy cellular infiltration without conspicuous hyaline membranes, focal hyperplasia of pneumocytes with only patchy cellular inflammatory infiltration. The pathological characteristics of the infected individual who died of COVID-19 indicated less fibrosis and consolidation with increased exudative COVID-19 damages **[32]**. Other studies indicated the damage of the alveoli in addition to cellular fibromyxoid exudates which indicated the occurrence of ARDS. The lymphocytes were found to be high with mononuclear inflammatory infiltrates; the flow cytometric studies of CD4+ and CD8+ T cells counts showed a drastic reduction and in turn these observations suggested the critical damage that has occurred in the immune system **[24]**. In few reports, the expression of ACE2 receptor protein in Asian male samples has shown an increase of about five times the expression of the same in the white and Afro-American samples **[33]**. Clotting disorders were observed in critically affected COVID-19 patients with increased in prothrombin time and D-Dimer levels, which further complicated the condition due to intravascular coagulation. It was also reported that there was an increased levels of CD3+ lymphocyte which further indicated the possibility of the immuno-suppression in the patients and a diligent use of corticosteroids in the COVID-19 treatment **[34]**.

Treatment

Infected individuals from SARS-CoV-2 need isolation, oxygen therapy for dyspnoea, rehydration management for dehydrated patients and appropriate use of antibiotics for sepsis is usually prescribed **[35]**. Routine administration of glucocorticoids is not usually recommended for SARS-CoV-2 patients unless there is some sign of complicated symptoms **[36]**. The use of intravenous immunoglobulin anibodies may benefit chronically to sick patients. Interestingly, the antimalarial drug, Chloroquine had shown promising inhibition of SARS-CoV spread due to its interference with the ACE2 receptors in the Vero E6 cell lines by reducing the severity of pneumonia,

improvement in radiological findings and reducing the duration of the disease. In United States of America, Remdesivir, a broad spectrum antiviral drug which was used for Ebola virus treatment was used to treat COVID-19 positive patients **[36]**. In a brief study on the combined therapy of antiviral drugs like Lopinavir / Ritonavir, Arbidol along with the Chinese conventional medication namely. Shufeng Jiedu Capsule (SFJDC), showed a remarkable improvement in three out of four COVID-19 patients **[37]**. Among the antiviral drugs used, the preclinical studies of remdesivir in comparison with that of lopinavir / ritonavir combined with interferon-β showed promising activity in reducing MERS-CoV affected mice model and further it helped in the improvement of lung tissues **[38]**. A recent report explored on the use of convalescent plasma as a possible treatment for treating COVID-19 infection **[39]**.

Control and Preventive Measures

The rise in the count of COVID-19 infected individuals across the world prompted the WHO to proclaim COVID-19 as a pandemic on 11th March 2020. Infected case isolation, quarantine and touch monitoring are considered crucial to prevent the further spread of the virus in hospitals and clinics. Suspicious cases with signs of symptoms such as sneezing, cough, dyspnoea and fever were advised to follow the respiratory etiquette and they should never be allowed to sit at the triage area along with other ill patients **[40]**. Most importantly, the medical and paramedical professionals were strictly advised to wear the protective gear like personal protective equipment (PPE), face shield, N 95 mask and their safe disposal as well. The health authorities quickly acted and isolated the affected people and the suspected people who were in close contact were quarantined Further transmission could be avoided by strictly following the social distancing norms between individuals, avoiding physical contacts, avoid crowding at public places and social functions among others. On 22nd March 2020, WHO further laid down strict guidelines for travelers and movement of goods from the affected regions to avoid the risk of transmission in the population and also provided sufficient updates on the conditions prevailing on that particular region. In order to identify the suspected COVID-19 individuals among the common public, thorough health monitoring system like temperature scanning, hand sanitization and wearing of face masks were insisted in the affected regions **[41]**.

CONCLUSIONS

It is observed from the literature reports that COVID-19 is a critical health threat at the international level. The task was rather challenging because of the nature of the virus, longer incubation period, high reproductive number, availability of limited treatment protocols, prevention of communal spread etc. Further, COVID-19 virus should be monitored periodically for any possibility of genetic variation or antigenic conversion to prevent the relapse of the infection among the population. In other words, there is a lot more of information that is needed to know about the epidemiological features of the virus to prevent the relapse at a global level.

Conflict of Interest

All authors declare no conflict of interest.

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