A Review: Pandemic Novel Coronavirus (COVID-19)

By Hariprasad M.G, Narayan Sah Sonar & Biki Ray

Abstract- The uncontrolled expansion of the novel coronavirus has stirred panic and unwelcoming sentiment and economic loss towards the world. The full spectrum of COVID-19 ranges from mild to severe respiratory illness with severe progressive pneumonia, multiorgan failure, and death. COVID-19 highly transmitted from person to person, thus need to the isolation of patients and maintain the quarantine. Lots of sought gain insights for vaccine design against SARS-CoV-2 (Severe Acute Respiratory Syndrome-Coronavirus-2) by considering the genetic similarities to SARS-CoV. This review article discusses the official updates on coronavirus, symptoms, transmission, diagnosis, reviews on pathogenesis, structure, treatment policy and our opinions on the use of drugs for the treatment of COVID-19 infection.

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I. INTRODUCTION

Contagious diseases like from herpes and legionnaire’s disease in the 1970s, to AIDS, Ebola, the SARS, and now COVID-19 continue to be dreadful and put pressure on human populations across the globe. Historians, who never lost enthusiasm for scourges, have a lot to offer.

SARS-CoV-2 is the reason for a continuous over the world outbreak of respiratory illness, known as coronavirus disease 2019 (COVID-19). It has confirmed that the virus is probably going to spread to most, if not all, nations. Regardless of terminology, this latest coronavirus disease is seeing increments in cases outside China. The 2019 novel coronavirus epidemic, which was first reported in December 2019 in Wuhan, China, and has been pronounced a general wellbeing crisis of global concern by the World Health Organization, may advance to a pandemic related with substantial morbidity and mortality. WHO has called the outbreak of SARS-CoV-2 infection as pandemic on 11 March 2020.

The chronology of COVID-19 diseases is as per the following. From December 18, 2019, through December 29, 2019, five patients were hospitalized with acute respiratory distress syndrome, and one of these patients died in Wuhan, China. On April 06, 2020, a total number of 1,285,257 positive cases among that 70,344 death cases reported. The COVID-19 is affecting 208 countries and territories around the world. (https://covid.worldometers.info/coronavirus/)

II. QUARANTINE

Quarantine is defined as separation and restriction of movement of well persons presumed to have been exposed to contagion. “Isolation,” in contrast, applies to the disunion of individuals who is known to be infected.

Even though, we are probably going to see more prominent utilization of vigorous social separating measures, such as school closures or the cancellation of public gatherings, broad sanitary cordons in which geographic areas were quarantined would bring up genuine protected issues. They also can present various logistical challenges and can expand the risk to those living in the restricted zone. Such measures may also have constrained adequacy with a highly contagious disease such as COVID-19.

At last, when governments confine individuals, they must meet those individuals’ essential needs, ensuring access to social insurance, medication, food, and sanitation. Such standards wasn’t constitutionally compelled: they are common to ensuring that detained persons agree to orders.

III. SYMPTOMS

The most widely recognized symptoms at the onset of COVID-19 illness are fever, cough, and fatigue, while different manifestations include sputum production, headache, hemoptysis, diarrhea, dyspnoea, and lymphopenia.

Clinical highlights revealed by a chest CT scan introduced as pneumonia; in any case, there were abnormal signs such as RNAemia, ARDS (Acute Respiratory Distress Syndrome), acute cardiac injury, and frequency of ground-glass opacities that led to death. At times, the multiple peripheral ground-glass opacities was observed in subpleural regions of both lungs that possible prompt both systemic and localized immune response that led to increased inflammation. Some of the cases shown an infiltrate in the upper lobe of the lungs that was related to increasing dyspnea with hypoxemia, through patients infected with COVID-19 developed gastrointestinal symptoms like diarrhea, a low percentage of MERS-CoV (Middle East Respiratory Syndrome-Coronavirus) or SARS-CoV patients experienced comparative GI distress.
IV. Transmission and Diagnosis

COVID-19 efficiently underwent replication in the upper respiratory tract and manifest a less abrupt onset of symptoms, the conventional human coronaviruses that are cause of common colds in the winter season. Virus undergoes replication in the upper respiratory tract and turn into large quantities during a prodrome period, are versatile, and carry on regular activities, adding to the spread of infection.

By contrast, transmission of SARS-CoV didn’t promptly happen throughout the prodromal period when those infected, and most transmission was thought to have occurred when infected individuals presented with serious disease, thus possibly making it simple to contain the episodes SARS-CoV caused, unlike the recent outbreaks with COVID-197.

COVID-19 also exhibits affinity for cells in the lower respiratory tract and can undergo replication where, causing radiological confirmation of lower respiratory tract lesions in cases who don’t present with serious disease, thus possibly making it simple to contain the episodes SARS-CoV caused, unlike the recent outbreaks with COVID-197.

V. Pathogenesis

Clinical and pathological discoveries in this critical case of COVID-19 cannot just assistance to determine a cause of death, but also gives new knowledge of the pathogenesis of SARS-CoV-2-related pneumonia, which might help physicians to formulate therapeutic strategy for similar patients and diminish mortality11.

Patients with SARS had a triphasic pattern of illness.

The first phase of illness, patients most frequently initially presented with fever, a nonproductive cough, sore throat, and myalgia, with dyspnea regularly not turning into a noticeable feature until days 7–14 of the illness.

During the second phase of the illness, dyspnea and hypoxia, with continued fever and frequently accompanied by diarrhea, became more prominent. Some patient’s respiratory status kept on disintegrating, and they developed ARDS required for mechanical respiration by the third week. The primary pathology observed at autopsy of patients that capitulated to contamination was diffuse alveolar damage.

The lungs of patients that died in the early phases of the infection contained hyaline membranes, edema, fibrin exudates, small vessel thrombi, loss and

**Table No. 1**: The systemic and respiratory disorders caused by COVID-19.

<table>
<thead>
<tr>
<th>Systemic Disorders</th>
<th>Respiratory Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. Fever</td>
<td>i. Rhinorrhoea</td>
</tr>
<tr>
<td>ii. Cough</td>
<td>ii. Sneezing</td>
</tr>
<tr>
<td>iii. Fatigue</td>
<td>iii. Sore throat</td>
</tr>
<tr>
<td>iv. Sputum Production</td>
<td>iv. Pneumonia</td>
</tr>
<tr>
<td>v. Headache</td>
<td>v. Ground-glass opacities</td>
</tr>
<tr>
<td>vi. Haemoptysis</td>
<td>vi. RNAemia</td>
</tr>
<tr>
<td>vii. Acute Cardiac injury</td>
<td>vii. Acute Respiratory Distress Syndrome</td>
</tr>
<tr>
<td>viii. Hypoxemia</td>
<td>ix. Sputum Production</td>
</tr>
<tr>
<td>ix. Dyspnoea</td>
<td>x. Lymphopenia</td>
</tr>
</tbody>
</table>

respiratory infection. SARS-CoV was dominantly transmitted through direct or indirect contact with mucous layers in the eyes, mouth, or nose of the infected individual. The fact that exposed mucous membranes and unprotected eyes expand the risk of SARSCoV transmission suggests that exposure of unprotected eyes to COVID-19 could cause acute respiratory infection9.

The clinical attributes of COVID-19 pneumonia in pregnant women was similar to those reported for non-pregnant patients who developed COVID-19 pneumonia10.

A COVID-19 is diagnosed by using reverse-transcriptase–polymerase chain reaction (RT-PCR) with primers and probes targeting the Orf1b and N genes of SARS-CoV-2.

The analysis proposes that the viral nucleic acid shedding example of patients infected with SARS-CoV-2 resembles patients with influenza and seems not quite the same as that found in patients infected with SARS-CoV. The viral load identified in the asymptomatic patient was like that in the symptomatic patients, which explain the transmission capability of asymptomatic or minimally symptomatic patients. These discoveries are similar with results that transmission might happen early in the course of infection and recommend that case detection and isolation may require strategies different from those need for the control of SARS-CoV4.
sloughing of pneumocytes, and a mixed cellular infiltrate of lymphocytes, macrophages, and polymorphonuclear leukocytes. Multinucleated giant cells that carried markers for macrophages and pneumocytes were often present.

At later phases of the disease, a histologic image of an organizing pneumonitis and consolidation, with type II pneumocyte hyperplasia, squamous metaplasia, and bronchiolitis obliterans was found. The relationship of worsening clinical progression with declining virus loads and the onset of an immunological response, in addition to the presence of markedly elevated cytokines levels, recommended that severe lung damage was largely immunopathological in nature.

VI. Structure of Virus

Coronaviruses were divided into three genera (alpha, beta and gamma coronavirus). Betacoronavirus demonstrated the potential for additional significant human diseases to result from coronavirus infections. For sure, soon after the identification of the SARS-associated human coronavirus (HCV).

COVID-19 symbolize the seventh member of the coronavirus family that affects in humans and also categories under the orthocoronavirinae subfamily. The COVID-19 forms a clade inside the subgenus sarbecovirus. Given the genetic sequence identified and the phylogenetic reports, COVID-19 is sufficiently different from SARS-CoV, and it would thus considered as a new betacoronavirus that infects people. The COVID-19 probably developed from bat influence coronaviruses. Another counter of proof that supports the COVID-19 is of bat origin is the presence of a high level of homology of the Angiotensin-Converting-Enzyme-2 (ACE2) receptor from a variety of animal species, thus implicating these animal species as conceivable intermediate hosts or animal models for COVID-19 infections.

The "coronavirus" is coined from the Greek word for crown, as under electron microscope, the virus envelope shows like crowned shaped which characterized by ring of small bulbous structure.

Coronaviruses are enveloped viruses with round and sometimes pleiomorphic virions of approximately 80 to 120 nm in diameter. Coronavirus contain positive-strand RNA, with the RNA genome about 30 kb. The genome RNA is complexed with the essential nucleocapsid (N) protein to shape a helical capsid found within the viral membrane. The membranes of all coronaviruses contain any of four viral proteins. These are:

i. Spike (S), the type I glycoprotein which forms the peplomers on the virus surface.

ii. The membrane (M) protein which transverse the membrane three times

iii. A short N-terminal a cytoplasmic tail and ectodomain, and

iv. A highly hydrophobic small membrane protein (E).

The E protein of IBV (Infectious Bronchitis Virus) has a short ectodomain, a transmembrane domain, and a cytoplasmic tail. The E protein of MHV (mouse hepatitis virus) was reported to transverse the layer twice, such that both N and C termini are on the inside of the virion. Some group II coronaviruses have an extra membrane protein, hemagglutinin esterase (HE). There is an additional group II virion protein called I for internal, as it was encoded within the nucleocapsid open reading frame (ORF) was a nonessential protein of unknown function. It has recently found that the ORF 3a-encoded SARS protein is an extra auxiliary protein. There might be other minor proteins, as yet undetected, included in virions.

The genomes of all coronaviruses have a comparable structure, about 20 to 22 kb carries the replicase gene, which encodes different enzymatic actions. The replicase gene products were encoded inside two broad open reading frames, ORFs 1a and 1b, which were translated into two polypeptides, pp1a and pp1ab, through a frame shifting mechanism involving a pseudoknot structure shaped by the genomic RNA. The basic proteins are encoded inside the three one-third of the genome, for all coronaviruses, in the order S-E-M-N. (When the HE protein was expressed, it is encoded 5 to S.) Each group of coronaviruses, in addition, encodes a group of unique small proteins; while these proteins are unnecessary and had been guessed to serve as accessory proteins and to interact or interfere with the host innate immune response, not shown for any of these proteins. The untranslated regions (UTRs) on either side of 5 and 3 ends of the genome, which were accepted to interact with the host and perhaps viral proteins to control RNA replication, which includes the synthesis of positive and negative strand genomic length RNA. Likewise, there are conserved sequences at the start of the transcription sites for each of the multiple subgenomic mRNAs; these are called transcriptional regulatory sequences (previously known as intergenic sequences). Coronavirus transcription was reviewed recently.
Fig. No. 1: Schematic diagram of the SARS coronavirus structure.

a) Structural Proteins of SARS-CoV-2 Are Genetically Similar to SARS-CoV

SARS-CoV-2 was observed to be near to SARS-CoV significantly more so than MERS-CoV based on full-length genome phylogenetic analysis, whether this is valid at the level of the individual structural proteins (S, E, M, and N). A direct reference arrangement based contrast indeed confirmed this, demonstrating that the M, N, and E proteins of SARS-CoV-2 and SARS-CoV had 90% genetic similarity, that of the S protein was prominently diminished (yet high). The resemblance between SARS-CoV-2 and MERS-CoV, then again, was significantly lower for all proteins, a feature that was also clear from the corresponding phylogenetic trees. We note that while the previous analysis was depend on the reference arrangement of each coronavirus, it was indeed a good representative of the virus, since less amino acid mutations was observed in the relating sequence data.

The percentage sequence identity with SARS-CoV-2 found as 76% S-protein, 96.6% N-protein, 91.1% M-protein, and 94.7% E-protein respectively compare with SARS-CoV.

VII. Treatment Policy

The first and most important is to isolate clinicians providing care from those making triage decisions. The “triage officer,” upheld by a group with expertise in nursing and respiratory therapy, would settle resource allocation decisions and communicate them to the clinical group, the patient, and the family.

Second, these decisions should be inspected routinely by a centralized state-level monitoring committee.

Third, the triage calculation had been reviewed consistently as information about the infections evolves. If decision not to intubate patients with COVID-19 for more than ten days, for instance, then discovered that these patients need 15 days to recover, we would need to change our algorithms.

VIII. Treatment Options/Therapeutics

The way of treatment included bi-daily oral administration of 75mg oseltamivir, 500mg lopinavir, 500mg ritonavir, and the intravenous administration of 0.25g ganciclovir for 3–14 days, another report indicated that the broad-spectrum antiviral remdesivir and chloroquine are exceptionally compelling in the control of COVID-19 infection. The National Medical Products Administration of China has approved the utilization of Favilavir, an antiviral drug, as a treatment for coronavirus.

However, lopinavir-ritonavir treatment did not significantly accelerate clinical improvement, reduce mortality, or diminish throat viral RNA perceptibility in patients with serious COVID-19. These information ought to advise future investigations to evaluate this and other medication in the treatment of infection with SARS-CoV-2. In this case of combining lopinavir–ritonavir with other antiviral agents, as has been done in SARS and is being studied in MERS-CoV, may upgrade antiviral effects and improve clinical outcomes remains to be determined.

There are considerable supporting the utilization of corticosteroids at a low-to-moderate doses in patients with coronavirus infection. According to the expert consensus statement, the accompanying essential standards ought to followed when utilizing corticosteroids:
The advantage and damage ought to have been carefully weighed before using corticosteroids; corticosteroids ought to have been used prudently in critically ill patients with COVID-19 pneumonia; for patients with hypoxemia because of underlying diseases or who routinely use corticosteroids for chronic condition, further use of corticosteroids should be careful; the dosage ought to be low-to-moderate (≤0.5–1 mg/kg per day methylprednisolone or equivalent), and the duration ought to be short (≤7 days).

IX. NOVEL CORONAVIRUS VACCINES AND DRUGS

(https://Covid.clinicaltrialsarena.com/analysis/coronavirus-mers-cov-drugs/)

Table No. 2: Therapeutic and prophylactic approach for novel coronavirus

<table>
<thead>
<tr>
<th>For all Vaccine and Drugs trail ongoing</th>
<th>Novel Coronavirus Drugs Approach</th>
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<tbody>
<tr>
<td><strong>Novel Coronavirus Vaccine Approach</strong></td>
<td><strong>Novel Coronavirus Drugs Approach</strong></td>
</tr>
<tr>
<td>a. Fusogenix DNA vaccine</td>
<td>a. OYA1, strong antiviral</td>
</tr>
<tr>
<td>b. Gimsilumab, human monoclonal antibody</td>
<td>b. Remdesivir (GS-5734)</td>
</tr>
<tr>
<td>c. AdCOVID, a single dose intranasal vaccine</td>
<td>c. Actemra</td>
</tr>
<tr>
<td>d. TJM2, a neutralising antibody</td>
<td>d. Galidesivir (BCX4430)</td>
</tr>
<tr>
<td>e. Virus-Like Particles (VLP) by Medicago</td>
<td>e. Regeneron</td>
</tr>
<tr>
<td>f. AT-100 (rhSP-D) a novel human recombinant protein</td>
<td>f. SNG001, natural Interferon-β</td>
</tr>
<tr>
<td>g. TZLS-501 a monoclonal antibody</td>
<td>g. AmnioBoost for ARDS</td>
</tr>
<tr>
<td>h. BPI-002 to activate CD4+ helper T cells and CD8+ cytotoxic T cell</td>
<td>i. Altimmune’s intranasal coronavirus vaccine</td>
</tr>
</tbody>
</table>

X. REPURPOSED DRUGS FOR TREATMENT OF COVID-19 INFECTION

a) Artemether–Lumefantrine and Amantadine

In this article, we recommend and request for emergency use authorization for Co-artemether (Artemether–Lumefantrine) and amantadine for treatment of COVID-19 infection18.

b) Local Antiseptic

Local antiseptic can wash of the throat infection of coronavirus, which further may prevent the SARS effects.

On going, German lab study supported by a manufacturer of povidone-iodine sore throat gargle, for instance, detailed that the solution was appeared to eliminate over 99 percent of the coronaviruses that cause SARS and MERS (very close cousins to the COVID-19). A prior Japanese lab study revealed that povidone-iodine products beat other antiseptics such as chlorhexidine gluconate and benzalkonium chloride in inactivating numerous other problematic viruses, such as coxsackie, rhinovirus, adenovirus, rotavirus, influenza. (https://COVID.nytimes.com/2020/03/29/well/live/gargle-gargling-coronavirus-infections-bacteria-virus.html)

XI. CONCLUSION

The transmission of COVID-19 can be preventing by, avoiding direct person to person contamination and maintaining well hygienic and sanitization. The research work for its diagnosis and treatment should bring out as soon as possible. Repositioning of drug efforts would be helpful in this emergency scenario as pharmacokinetics and pharmacodynamics of the drug are known.

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Conflict of interest: None

REFERENCES


