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CORONA PANDEMIC: OVERVIEW ON SYMPTOMS, CONTROL, DISINFECTION, TRANSMISSION AND TREATMENT

B. Lahiri[1]*, C.S. Lakshmeesha[1]

[1]Department of Pharmaceutical Regulatory Affairs, Acharya &BM Reddy College of Pharmacy, Bangalore, Karnataka - 560107, India

***Corresponding Author E-mail:** lahiri145@gmail.com

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ABSTRACT

Corona disease has emerged as a pandemic of global proportions. COVID-19, the causative viral species of the coronavirus has been found to be of zoonotic origin. Corona disease has spread to 210 countries, affected more than 24 million people and caused more than 820,000 deaths. COVID-19 viruses propagate mainly by droplets infection. COVID-19 is similar to SAR-COV. Corona disease is characterized by respiratory illnesses such as common cold, difficulty in breathing and pulmonary edema. These symptoms are similar to those reported in Middle East Respiratory Syndrome or Severe Acute Respiratory Syndrome. The United States and Europe have half of the global infections. However, the infection is spreading rapidly in Asia and South America. Comprehensive measures have been taken to mitigate the outbreak and reduce inter person transmission of COVID-19. Vulnerable populations (kids and elderly people) require more attention and efforts to reduce transmission. This paper discusses etiology, symptoms, disinfection and treatment available for COVID-19 infection. It outlines different studies conducted to understand the mode of transmission and repurposing of drugs for the treatment of the disease. Preventive measures have been mentioned in brief. A positive outcome has been the successful repurposing of drugs such as remdesivir, favipiravir, convalescent plasma, hydroxychloroquine, ribavirin, chloroquine phosphate, tocilizumab, dexamethasone and IFN-α for the treatment of COVID-19 infection.

INTRODUCTION

Corona disease has emerged as a major respiratory disease. The previous upsurge of coronavirus (CoV) involves extreme (SARS)-CoV and (MERS)-CoV, previously identified as agents that present a significant danger to public safety. At the end of the year 2019, a patient outbreak was diagnosed via an initial diagnosis of unknown etiology of pneumonia. It was epidemiologically linked to the retail market for seafood and wet items in Wuhan, China. Initial results forecast the emergence of Possible Coronavirus epidemic, focused on the 2019 New Coronavirus (named as COVID-19 by WHO on Feb 11, 2020) expected to be substantially greater than 1 (ranges between 2.24 to 3.58). [1] These were named coronaviruses since they are circular virions with a central shell with surface structures like a solar crown. There are four subfamilies among coronaviruses, including beta-, alpha-, gamma, delta. Alpha-, β –-coronaviruses tend to occur from mammals, particularly bats,

gamma, delta, have been shown to originate among pigs, birds. The scale of its genome varies from 27 kb to 33 kb. Beta-coronavirus is a cause of severe disease including fatality of the 7 coronavirus subtypes that may affect humans, while alpha-coronavirus induces symptomless to mild systemic infections. SARS-CoV-2 is part of the B branch of beta-coronavirus which closely relates to SARS-CoV.[2]

ETIOLOGY

The glycoprotein known as viral spike (S) covalently binds to its corresponding target cell receptor, a protease enzyme in the host body. This stimulates the spike protein bonded to the receptor and the infection begins. The procedure of cleavage formation and stimulation enables the viral units to reach their target cell through endocytosis as well as direct membrane fusion.[2] Presence of a 5′ methylated tip, as well as a 3′ polyadenylated end, have been found in the COVID-19 genome. The viral units become uncoated before they reach the target cell. The viral genome reaches the cell cytoplasm causing translation at 10th position and formation of a long chain polyprotein that divides the chain into several non-structural proteins. Coronaviruses are encased, positively single-stranded, large RNA viruses which cause disease, and often have the capacity to infect other species. Tyrell and Byone provided the first definition of the virus in 1966 after a study on the virus among patients experiencing colds and flu.[3]

SYMPTOMS

Infection with COVID-19 happens at about 5.4 days after coming in contact. The time from the start of symptoms to a death varies from 6 to 40 days with 15 days being the mean. This duration relies on the age and state of the immune system of the individual. A shorter span of time has been found for individuals aged more than 70 years.[4] The most prevalent signs just at the start of sickness include cough, fever and weakness, and other signs such as sputum development, emesis, hemoptysis, nausea, lymphopenia as well as dyspnea. Although the clinical characteristics of CT scan of the chest have been described as pneumonia, other unusual aspects such as RNAaemia, severe respiratory distress syndrome, acute cardiac failure and occurrence of large-glass opacities contribute to death. In several instances, many peripheral large-glass opacities have been found in both subpleural lung regions which are likely to induce widespread and localized inflammatory responses contributing to increased inflammation.[1]

CONTROLLING COVID-19

Both case isolation and touch tracking are used to monitor infection transmission (COVID-19). The ability of this technique to monitor relies on the features from both the disease as well as the responses. This is a code study to see whether insulation and interaction control will regulate the diffusion of COVID 19 incidents. Pronounced as “R naught”, R0 is the reproduction number. It is meant to be a measure of the transmissibility or infectiousness of an infectious disease. R0 is usually mentioned in the scientific and healthcare publications and can also be seen in the mainstream press.[5]If R0 (reproduction number) increases above 1, it means that a single infected person is capable of spreading the disease to more than 1 person and so on. This makes the disease a contagious one from a statistical standpoint. When R0 is less than 1, it means that a single infected person spreads the disease to less than 1 person that gives a decreasing trend to the disease.[6]The possible severity of a contagious disease is often measured by R0. The latter can be used to measure the percentage of the population to be immunized in order to eradicate the infection. The R0 values for polio, Ebola virus, measles, AIDS disease, influenza and various other communicable diseases have been published.[5,6]R0 values for various diseases are as follows.[5,6]

1. Measles – 12-18
2. Pertussis – 12-17
3. Diphtheria – 6-7
4. Polio – 5-6
5. Small Pox – 5-7
6. HIV/AIDS – 2-5
7. SARS – 2-5

The likelihood of disease monitoring has been found to be greater with the number of initial cases of R0 being 2·4 to 3·6 and reduced transmission before the emergence of symptoms. Simulated incidents with 5 set initially, R0 with 1·3, 0 % transmission may

also be tracked via a small possibility of interaction monitoring. From across original series of incidents, the bulk of situations from an R0 of 1·6 have been tested with just positive monitoring of fewer than 50 % of contacts.[7] Upwards of 70% of incidents have been traced in R0 of 2·6 to monitor the bulk of outbreaks and over 90% in R0 of 3·4, respectively. The time since the initiation of symptoms as well as isolation played a very significant function in determining if a 1·6 epidemic of R0 is manageable.[4] As mentioned in Fig.1.[4] The proportion of incidents reported for situations having specific reproductive quantities (R0) at escalated touch frequency. The baseline scenario looks like R0 with 2·6, 20 at first fixed, brief ventilation period, 17% transmission leading to symptoms appearing and 0 times higher subclinical infection. A modelled outbreak is defined as managed when there are no more cases between weeks 12 and 16 following the initial cases.[4] As mentioned in Fig.2.[4] Effective percentage of reproduction, if case isolation and contact tracing are present. The median periods are 50% to 95%. Control (or controlled) epidemic has been identified as non-occurrence of new disease between 12 weeks and 16 weeks after primary diagnosis. Basing on the concept of coronavirus 2 similar pathogens, they (stated that an occurrence of the extreme acute respiratory syndrome was regulated for each scenario during 12 weeks, providing the specific reproductive number was constant but no further action was undertaken.[4]

DISINFECTION

In observation of histopathologists, doing research on coronavirus is interesting. While working with morbid tissue samples, they found the task of making coronavirus lose it's a pathogenic activity an extremely tough work. Inhibition of Corona Virus-2 (SARS-CoV2) may be accomplished in histopathological research labs by implementing one of the following procedures or even a combination of them.[8]

1. Ethanol 60-70% or higher, as in procedures for tissue preparation.[8]
2. One-minute exposure to sodium hypochlorite solution 0.1 – 0.2% or hydrogen peroxide 0.5 – 1% solution works.[8]
3. Chlorhexidine digluconate solution 0.02 – 0.05% and benzalkonium chloride 0.06 - 0.3%, are not preferred on inanimate surfaces, as they turn out to be less effective.[8]
4. U.V Radiation's application on microbial culture close to 1 hour can lead to a reduction of COVID 19 manifestation to a substantial low threshold.[8]
5. Preserving the morbid tissues in formalin or even in glutaraldehyde for 25 hours or 25-50 hours.[8]
6. Heating the tissue at various temperatures for a specified timeframe throughout histological tissue treatment.[8]

This virus has been documented as possessing 70 - 85% similarity to SARS-CoV with predominantly mode of transmission through inanimate surfaces and broad droplets. Even in the labs dealing with coronavirus should be using detergents as well as disinfectants. Alcohol-based disinfectants in general, ethanol-based in particular, should be properly rinsed out and sanitized through the use of ethanol.[9] Since the virus is extremely contagious and dangerous, a wide array of biological disinfectant products must be recognized and used for inactivation.[10]

FINDINGS

Higher leukocyte rates, irregular breathing observations and elevated plasma rates of proinflammatory cytokines have been recorded in patients suffering due to COVID-19. In one case of COVID-19, even a patient with only a 5.5 days history of fever has been diagnosed with cough, coarse tones within the lungs and shown to have a temperature of 39.2°C. A diagnosis of the patient's sputum confirmed COVID-19 infection based on the polymerase chain reaction in real-time (RT-PCR).[11] Extreme pneumonia, RNaemia as well as the prevalence of ground-glass opacity and aggressive heart trauma have been considered as main pathogenesis for COVID-19 infectious disease as the virus targets the respiratory system.[12] COVID-19 has been classified as Category 2B β CoV, by the (WHO). Out of a total of 9 patients, 10 genome-19 sequences

showed a 99.98% sequence similarity. The sequence research results performed in isolates taken from 5 patients revealed not only a 99.70–99.98% nucleotide identification amongst the detected viral strains but also a new beta-CoV strain identified in.The phylogenetic evidence shows however that COVID-19 belongs to the beta-coronavirus class, that comprises SARS-CoV infecting human beings, animals as well as livestock.[13]

TREATMENT

Chen N et al.have reported about a treatment given to 75 patients using currently available anti-viral drugs such as oral administration of oseltamivir 70mg, lopinavir 600mg, ritonavir 400mg and intravenous administration of ganciclovir 250mgfor 4–15 days.[14] In an in vitro regulation of the infection of 2019 n CoV, a large-scale antiviral study found both remdesivir and chloroquine are found to be highly efficient. The safety record in human patients has been established for these antiviral compounds. The treatment of COVID-19 can be conducted using these as medicinal agents.[15] Faced with the daunting outlook of the COVID-19 disease outbreak spike coupled with inadequate in-patient beds, health care and services staff, it has become crucial to monitor and treat the sick and elderly in a safe as well as secure manner. The ongoing epidemic can be considered as a creative thinking incentive to evolve as well as adapt a generally slow-moving health system to a more proactive and crisis management oriented one on the basis of the pandemic remote technology can reduce the burden on health care facilities by using it to manage the COVID 19 subjects who are severely ill and can minimize risk to the health workers. Its use should, however, be counterbalanced by the emphasis on privacy protection as well as cyber safety. Remote patient surveillance might have the following advantages in curbing the pandemic.[16]

1) Flexible, agile and much more cost-effective system.[16]

2) Allows skilled Intensifiers to remotely track the condition of several ICU patients on the internet-enabled phone or computer setup.[16]

3)Ensures constant control of critical physiology 24x7.[16]

4) The abrupt clinical decline may be identified sooner, and on-site physicians may be notified to take or administer appropriate action as needed within a short time frame.[16]

5) Guarantees quality patient care with minimal human interactions and financial resources.[16]

Enables quarantine situations and areas to be monitored from an off-site location.[16]

As shown in Table 1.[16] Until enough detailed therapeutics are available to the public, it's indeed necessary to suggest more broad-spectrum antivirals which include medication therapy choices for infectious disease such as COVID-19, such as Lopinavir, Neuraminidase inhibitor, Ritonavir, peptide (EK1), RNA synthesis blockers.[16,17]Even so, further research is needed to understand while trying to identify new chemotherapies for the treatment of infectious diseases like COVID-19.An experimental animal template can be used to reproduce the dangerous disease currently seen in humans and is desperately required to improve on pre- and post-exposure prophylaxis against the virus.[1] Favipiravir is, in fact, a drug which earns interest compared to just the drugs mentioned above, which have been mentioned in the regulations. Favipiravir was certified for treatment against the novel flu in China around February 2020. The medication is undergoing significant clinical studies in the treatment of COVID-19. Favipiravir falls under a new sub-type of RNA-dependent polymerase blocker (RdRp). In contrast to antiviral activity, favipiravir also prevents the replication of alpha, flavi, bunya, filo, noro-, arena and various other RNA viruses.[18]

CHINESE MEDICINE:

Although the novel study of COVID-19 emanates from Wuhan City, China, a multitude of conventional treatment such as the evacuation of lungs and medications including *Shuanghuanglian* orally administered liquid that potentially prevents the symptoms of SARS-CoV-2. In a prior study paper, it was observed that chlorogenic acid, baicalin, forsythine in *Shuanghuanglian* orally administered fluid had some indication of a mitigatory action on a number of harmful bacteria and viruses. The explanation might just be that these, certain elements have performed a preventive role while selectively

decreasing the body's immune reaction to viruses and bacteria by reducing inflammatory reactions.[19] A traditional/conventional Chinese medicine known as *LianahauQuinghwen* capsule has been shown to have a broad-range impact on a variety of viral diseases, which include H7N9, also possibly could regulate the inflammatory response to the virus which would lead to a significant reduction in the amount of inflammatory reactions from a veryearly stage of the viral disease.[20]

CHALLENGES IN VACCINE DEVELOPMENT

The worrying fact being that out of the hundreds of clinical trials that have been conducted and few ongoing since the outbreak of the pandemic, an effective antiviral therapy has not yet been developed. This creates an immediate need to vaccinate a majority of the population against the COVID-19 infection. More than 100 Coronavirus vaccine candidates are presently undergoing development and this figure has been growing.[21] However, this is turning out to be a very difficult task because the development of a safe and reliable vaccine needs rigorous and detailed testing before regulatory approval. Moreover, commercialization of approved vaccine will present its own gigantic challenges in terms of production, logistics and administration by healthcare professionals to the whole of mankind. The developing countries pose more complex challenges due to ill-developed healthcare systems and funding as well as logistic issues. They have the majority of the human population on earth and also people with low purchasing power.[21]

Vaccine types currently being considered for Covid-19:

1. Inactivated Vaccines – Highly developed manufacturing process but requires live virus handling.[21]
2. Immunity based vaccine – Possibility of boosting innate immunity against a variety of infectious agent.[21]
3. Live attenuated vaccines - Produces very robust immune response, is long-lasting.[21]
4. Recombinant vector and protein-based vaccines - May need additional adjuvants. Mostly safe produce strong immune response.[21]

The continuous mutating nature of the coronavirus has led to change in symptoms and its effect on the human body depending on the geographical area. This has led to the reduced therapeutic efficacies of the recommended drug therapies and increased recovery time or higher infectious rate even higher mortality rate.[21,22]Thus, a vaccine has to produced and administered as soon as possible for us to overcome this pandemic without plunging into further loss in quality of life. But the changing nature of the virus candidate is might prove to be a challenge to the scientists and health care workers in developing a mitigative or preventive measure.[22]

RE-PURPOSED VACCINESFOR COVID-19:

Authorized and regulated vaccines, which include BCG and Polio vaccine have shown to possess unspecific, immunoregulatory effects on the immune system as well as provide immunity against a few infectious diseases.[23] This has contributed to the idea that such vaccines may also have an impact on protection from Coronavirus.[24] BCG vaccine is undergoing multi-centre randomized clinical trials in Australia, South Africa and the Netherlands taking the health care staff under consideration.[23,24]The measles vaccine is being considered to suppress Coronavirus infection in health care staff in Egypt and the trial has been authorized. In the USA Oral Polio vaccines have been proposed as repurposing candidate in the prevention of COVID-19.[23]

Concerns in the post vaccinated era:

These are the following:

1. Uncertainties about the duration of immunity developed against Covid-19 due to vaccination,
2. Possibilities of mutation in Covid-19

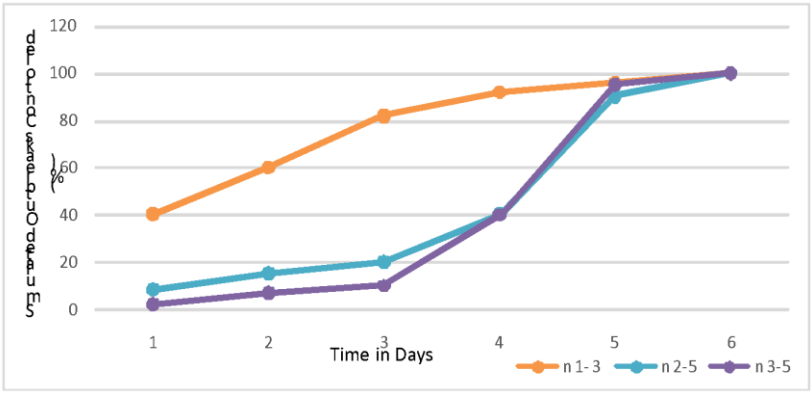

Fig. 1 Sample of the simulation cycle beginning with infection of individual A[4].

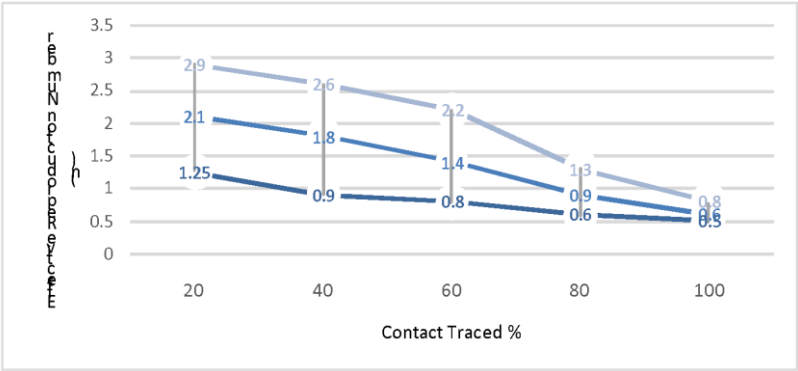

Fig. 2 Impact of isolation and contact surveillance on preventive measures and effective N[4].

Table 1: Antivirals Tested For The Treatment Of Covid-19 Infection.[16]

Medication	Required Dose / Day	Administration	Time
IFN-α	6 million Units or similar dosage every time, twice	Vapour	Up to ten days
Lopinavir / Ritonavir	300 mg / 40 mg / tabs, 2 tabs every time, twice	Oral	Up to ten days
Ribavirin	400 mg each time, 2-3 times/day in combination therapy with IFN-α or lopinavir/ritonavir	I.V. Infusion	Up to ten days
Chloroquine phosphate	400 mg (200 mg for chloroquine) at a time, twice	Oral	Up to ten days
Arbidol	300 mg every time, thrice	Oral	Up to ten days

CONCLUSION

SARS-COV2 has spread extensively since its identification in Wuhan. It has shown to have a wide array of severity when assessed on the following parameters,

1. Confirmed cases,
2. Casualties,
3. Recovered cases,
4. Re-infected cases

Going by the number of cases, the USA, Brazil, Russia, India, Peru, Chile, Spain, Italy and Iran are the most affected states in the World. In general, the spread of the virus is increasing daily in the continents. The number of cases of COVID-19 is rising rapidly in densely populated countries. Vaccines are not yet available for this disease. Therefore, preventive measures as per WHO recommendations have to be followed seriously to reduce the intensity and spread of this infectious disease amongst volunteers and healthcare professionals

involved in research and clinical trials as well as treating the infected people. Epidemiological changes should be monitored in the COVID-19 populations in light of potential pathways for transmission and clinical infections, mutations, viral growth and transmission among humans or possible species as the disease reaches and infects various different species.[1] The non-availability of medicines for the treatment of Corona disease necessitates assigning highest priority for early development of a vaccine. The development of a vaccine for a pandemic like Corona will have gigantic challenges which involve compliance to regulatory requirements, commercialization at the global level and post-development concerns related to the longevity of immunity induced by it and possible mutations in the viral genome. Many questions are still to be clarified with the evidence and tests. This includes details about who and how many have been screened and tested, how much traceability of contact has been made, and what proportion of these screened candidates has been positive and if this statistic remains constant or varies with time. The forthcoming months are more crucial than the earlier ones for the prevention and mitigation of this pandemic.

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