Critical Insight into the Attributes of Emerging Novel Coronavirus (COVID-19) in India and Across the World

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Abstract: The World Health Organization (WHO) has recently announced the spread of novel coronavirus (nCoV) globally and has declared it a pandemic. The probable source of transmission of the virus, which is from animal to human and human to human contact, has been established. As per the statistics reported by the WHO on 11th April 2020, data has shown that more than sixteen lakh confirmed cases have been identified globally. The reported cases related to nCoV in India have been rising substantially. The review article discusses the characteristics of nCoV in detail with the probability of potentially effective old drugs that may inhibit the virus. The research may further emphasize and draw the attention of the world towards the development of an effective vaccine as well as alternative therapies. Moreover, the article will help to bridge the gap between the new researchers since it’s the current thrust area of research.

Keywords: Novel coronavirus, SARS-CoV-2, nCoV, COVID-19, global impact, signs, symptoms.

1. INTRODUCTION

Coronavirus (CoV) is a broad virus family ranging from the common cold to Middle East Respiratory Syndrome (MERS) coronavirus and Severe Acute Respiratory Syndrome (SARS) coronavirus. Recently, a novel coronavirus (nCoV) strain has been identified, which was not found in humans previously. Uniquely, CoVs (order Nidovirales, family Coronaviridae, subfamily Coronavirinae) are enveloped viruses present in the RNA genome. The genome size of CoV that ranges from 26 to 32 kb is considered as the largest genome for an RNA virus. Eventually, CoV has been classified into four categories, as α-CoVs, β-CoVs, γ-CoVs, and δ-CoVs based on its criteria of antigenicity and genetic makeup. [1]. Six human coronaviruses (HCoVs) have been found and identified to date, which include two α-CoVs (HCoV-NL63 and HCoV-229E) and four β-CoVs (HCoV-HKU1, HCoV-OC43, Severe Acute Respiratory Syndrome-CoV, and Middle East Respiratory Syndrome-CoV) [2]. Even though the exact transmission mechanism of SARS-CoV and MERS-CoV has not been established clearly, it has been suggested that SARS-CoV transmitted from civet cats or bats to humans and MERS-CoV transmitted from dromedary camels to humans [3]. The nCoV strain discovered with the probability of potentially effective old drugs that may inhibit the virus. The research may further emphasize and draw the attention of the world towards the development of an effective vaccine as well as alternative therapies. Moreover, the article will help to bridge the gap between the new researchers since it’s the current thrust area of research.

2. TRANSMISSION OF DISEASE

Coronaviruses are zoonotic, meaning that it is transmitted between animals and humans. Nevertheless, it has not yet been identified whether nCoV actively spreads from animals to humans but the mode of transmission between individuals is established. Disease transmission occurs through fomites and droplets of bodily secretions, including mucus or
infector saliva. Sneezing or coughing occurs in the dispersion of these droplets onto air or surfaces. For instance, when the person with the virus sneezes or coughs, the mucus or saliva is carried into the air about 6 feet or higher [12]. Furthermore, scientific literature suggests that the spread of nCoV is not only limited to airborne transmission, but also through the fecal-oral route. However, the fecal-oral route does not appear to be a major factor in the transmission of disease. Transmission of the virus is a major health risk when transporting since the virus could settle on the surface and survive before it comes into contact with the live host [13]. Evidence suggests that the virus is transferred less from smooth surfaces than from hard surfaces such as a doorknob. Most estimates of the incubation period of nCoV range from one and fourteen days, most commonly around five days. Surprisingly, an asymptomatic person may also shed virus that may be potent for transmission [2, 14, 15]. In due time, there are no reports of animals (pets) playing a significant role in spreading the virus. On the contrary, the risk of animals (pets) spreading the virus to humans is considered to be low. In the United States, a tiger is believed to have contracted the virus from an exposed zoo employee who was found to be Coronavirus disease of 2019 (COVID-19) positive. Further studies are needed to understand the transmission mechanism of the virus among different animals [16, 17].

3. SIGNS, SYMPTOMS AND CLINICAL FEATURES OF COVID-19

The signs and symptoms of COVID-19 are unspecific and the nature of the disease may vary from absence of any symptoms to severe pneumonia and death. After the exposure to the virus, symptoms appear to begin with fever, accompanied by dry cough, fatigue on 5th to 6th day (Mean incubation period: 5-6 days) and may vary between 1-14 days [9, 18]. 80% of COVID-19 infected patients have a moderate condition that involves cases of non-pneumonia and recovery. Significant diseases such as pneumonia, dyspnea, and difficulty in breathing are present in 13.8% of patients with severe conditions. Whereas, respiratory disorders, septic shock, acute heart injury, and multi-organ failure are present in 6.1% of patients with critical condition. However, some of the symptoms, such as sputum production, confusion, headache, hemoptysis, and diarrhea, are rare [9, 19, 20]. Older adults and the people suffering from the underlying medical conditions including heart disease, diabetes, or asthma are more prone to getting infected with the virus [21]

Laboratory observations demonstrate lymphopenia with reduced lymphocyte count and enhanced levels of neutrophils and white blood cells in severe and critical patients. Certain uncommon laboratory results indicate elevated serum C-reactive protein levels, D-dimer, lactate dehydrogenase, alanine transaminase, erythrocyte sedimentation levels, and procalcitonin correlated to severe patients compared to non-serious patients [9, 19, 22, 23]. Comparatively, severe, and critically ill patients had elevated inflammatory factors [24]. Consequently, blood urea and creatinine levels increased substantially until death as the disease escalated and worsened its clinical condition [25].

A study demonstrated that patients with hypertension have 2.27- and 3.48-fold higher risks of severity and fatality compared to COVID-19 patients without hypertension. Until now, the exact mechanism of hypertension as a risk factor for acquiring COVID-19 is unclear. The patients suffering from COVID-19 with hypertension are usually treated with angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers. On the contrary, the virus causing COVID-19 binds to ACE2 receptors in the lungs, which raises a question of whether these agents are harmful or beneficial in the treatment of nCoV [26, 27]. Patients infected with COVID-19 have a high risk of developing venous thromboembolism (VTE), a cardiovascular or respiratory complication. Notably, 25% of COVID-19 cases are associated with VTE in the intensive care unit and contribute to the high mortality rate in patients. The probable correlation between thrombosis and COVID-19 is that the virus causes massive inflammation boosting cytokines, which in turn increases the generation of clotting factors in the liver [28, 29]. The nCoV spreads through the respiratory system and may cause pneumonia with profound breathlessness and hypoxia. Ultimately, people with underlying medical conditions have a higher risk of contracting the infection, which may be associated with acute respiratory distress syndrome (ARDS). At present, the correlation between COVID-19 and ARDS is unclear. Under those circumstances, severe respiratory failure is more likely the cause of death in COVID-19 patients. Hence, timely mechanical ventilation is mandatory to prevent patients progressing from a mild disease to more severe lung injury [30, 31].

The progression of severe illness with COVID-19 is mainly intense with no significant distinction between severe and critical illness (Table 1). Such patients are treated in the early stages of critical illness in the Intensive care unit (ICU). However, not all patients with critical illness need intensive care. Most of the critical cases with COVID-19 were older patients with the presence of comorbidities, including diabetes mellitus, hepatic, cardiac, chronic lung disease, and cancer. Moreover, ARDS, disseminated intravascular coagulation, septic shock, and multiple organ failure may progress quickly in some cases. According to the reports, the ICU mortality rate of COVID-19 patients was particularly higher than normal death rates for critical care settings.

Table 1. Classification of severity of COVID-19 cases

| nCoV Cases with Severe Illness | nCoV Cases with Critical/Life-Threatening Illness |
|------------------------------|-----------------------------------------------|
| Anhelation with respiratory rate ≥ 30 times/min;| Respiratory failure, Shock, Multiple organ failure, encephalopathy, myocardial injury or heart failure, acute kidney injury |
| Oxygen saturation at rest <93%; PaO2/FiO2 <300 mmHg | |

4. THE GLOBAL SPREAD OF COVID-19

On the 31st December 2019, 27 cases of pneumonia of unknown etiology were identified in Wuhan City, Hubei province, in China. The causative agent was identified from throat swab samples conducted by the Chinese Centre for Disease Control and Prevention (CCDC) on the 7th January
2020, it was subsequently named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and later named COVID-19 by the World Health Organization (WHO) [8, 32].

The current outbreak of the novel coronavirus SARS-CoV-2 has spread to many other countries globally. Since then, the WHO declared the Chinese outbreak of COVID-19 to be a Public Health Emergency of International Concern posing a high risk to countries with vulnerable health systems [33].

Surprisingly, more than 1610909 cases of COVID-19 have been confirmed so far, and over 99690 among these were dead between 21st January and 11th April 2020 (Fig. 1). In fact, more than 200 countries across the world have reported cases of people getting infected with CoV [7].

There is a steady rise in the daily total number of COVID-19 cases across the globe. As of April 2020, the United States of America bears the largest burden of morbidity and mortality, whereas the incidence in other Asian countries, in Europe and North America, has been increasing drastically. Table 2 describes five countries with the highest number of confirmed cases, deaths and fatality rate, globally [34, 35].

5. CONFIRMED CASES OF COVID-19 IN INDIA AND ITS RESPONSE

A total of 7447 cases have been confirmed (Fig. 2) and the virus has led to deaths of 273 patients across India as of 11th April 2020. The number of cases is growing rapidly across various states of India, of which Maharashtra state has been infected badly with 1761 cases [36].

The infection rate of COVID-19 in India is reported to be 1.7, which is significantly lower than the worst affected countries. Moreover, on 22 March 2020, a 14-hour voluntary public curfew was held, which was followed by a nationwide lockdown for 21 days [37, 38]. In the states affected, there is an ongoing hospital isolation of the patients, along with the tracing and household quarantine of their contacts. For instance, a total of 1,61,330 samples from 1,47,034 individuals have been tested across India as of 10th April 2020. In addition to the ICMR-National Institute of Virology, Pune, 51 Virus Research and Diagnostic Laboratories (VRDLs), and the National Center for Disease Control, COVID-19 are designated to facilitate sample collection. Besides, a total of 159 government laboratories and 69 private laboratories are assigned for testing of COVID-19 across India [39]. India has also set up a make-shift laboratory in Iran to test Indian citizens for nCoV before evacuating them to India for which

![The chronological incidence of confirmed COVID-19 cases and deaths](image)

**Fig. (1).** The chronological incidence of COVID-19 infections and death cases globally from 21st January to 11th April 2020.

**Table 2.** Top five countries affected by COVID-19 as on 11th April 2020.

| Countries | Confirmed Cases | Death | Fatality Rate |
|-----------|----------------|-------|---------------|
| USA       | 461275         | 16596 | 3.59%         |
| Spain     | 157022         | 15843 | 10.08%        |
| Italy     | 147577         | 18851 | 12.77%        |
| Germany   | 117658         | 2544  | 2.16%         |
| France    | 89683          | 13179 | 14.69%        |
it has received praise from the US government [40]. India has also sent medical supplies to China for tackling the outbreak of nCoV and suspended visas to prevent the further increase in the spread of the disease [41, 42]. It is thus seen that the Indian government is making all the possible measures to prevent the spread of disease activity in India and around the world.

The Indian Medical Research Council (ICMR) urgently requested approval from the DCGI for the restricted use of ritonavir and lopinavir in combination (anti-HIV drugs) for the treatment of COVID19. As per the official record, the informed consent is to be obtained from the patients before the treatment, and later on, the National Taskforce recommended the use of Hydroxy-chloroquine as a prophylactic agent against SARS-CoV-2 infection [43]. Eventually, this combination with other medications was used for the treatment of patients affected by the infection in China and Thailand [44]. Under those circumstances, several countries reached out to India to seek medical aid against the nCoV. Without delay, India being a leading market in generic medicine, approved to send hydroxy-chloroquine tablets to thirteen countries, including the United States [45].

6. ROLE OF RECEPTORS IN nCoV

The protein structures like the envelope protein, membrane, nucleocapsid protein, and the spike protein play a vital role in the entry of the virus and its replication into the host cells. The sequence of nCoV incorporates the receptor-binding motif (RBM), which indicates a strong binding interaction with the ACE2 receptor and thus confirms that nCoV utilizes ACE2 as its binding receptor. To emphasize, various residues present in nCoV RBM (specially Gln493) provide interaction to bind to the ACE2 receptor showing that the virus has a capacity for causing human infection. The Asn501 residues present in the nCoV RBM show some compatibility of binding with the human ACE2 receptor, thus confirming that it does have the capacity to cause human-human transmission [46]. Out of the fourteen contacting residues of ACE in the RBD (receptor binding domain), nine of them are conserved completely from the humans, bats, and civets. Evidence shows ACE2 as a receptor for nCoV, which is surrounded by five residues that undergo a natural selection in the case of SARS-CoV. Notably, the ACE2 surface receptor plays an important role in the cross-species transmission of the infection. Similarly, such processes of natural selection are presumed for its cross-species transmission in the case of nCoV. The process of the host cell entry of the virus starts with the interaction of RBD located in the S protein and the target receptor ACE2 [47]. Furthermore, the RBM located in the RBD of the S1 subunit of spike proteins interacts with the surface receptor and leads to the attachment of the virus into the host cells. The specific neutralizing monoclonal antibody binds to the ACE2 receptor and blocks the viral entry. To emphasize, effective treatments that can be used against nCoV are based on the use of either broad-spectrum antiviral drugs or specific therapeutic molecules. Such agents can directly interrupt any stage of the viral lifecycle or the receptor proteins located in the host cell surface to restrain the binding of the virus thereupon, blocking the virus attachment and entry [48]. Fig. (3) summarises the life cycle of the various stages of the virus.

7. POTENTIAL INTERVENTIONS

Several antivirals and immunomodulators that are reliable and safe for COVID-19 are being investigated without delay. To point out, antiviral agents are more likely to be given early after symptoms begin or as a preventive measure [49]. Remdesivir is an adenosine nucleotide analog with a significant antiviral action toward a wide range of RNA viruses. Eventually, phase III clinical trials in the United-States were conducted to assess the safety and effectiveness of remdesivir in COVID-19 patients in March 2020. In contrast, no intervention has been approved. [50–52]. Chloroquine increases the pH of the endosome required for viral fusion and interferes with the glycosylation of cellular receptors of SARS-CoV. Likewise, hydroxychloroquine has a similar mechanism of action, and these agents have an anti-viral and anti-inflammatory action that represents the primary intervention of SARS-CoV-2 [53–55]. Furthermore, clinical trials are undertaken for HIV protease inhibitors lopinavir and ritonavir, which inhibit viral replication. They are either given as a monotherapy or in combination with ASC09 (experimental HIV-1 protease inhibitor) with or without Arbidol, which has demonstrated antiviral activity in cell cultures against SARS pathogen [56–58]. Oseltamivir and other neuraminidase inhibitors were effective as an experimental treatment for MERS-CoV infection and have been widely used in COVID-19 patients in China, regardless of any accurate evidence of their efficacy [59, 60]. Also, Azvudine, an experimental reverse transcriptase inhibitor against HIV, is used in the most recent clinical trials as well [61]. In conjunction with Baloxavir marboxil (Cap-dependent endonuclease inhibitor) and favipiravir (guanine analog RNA dependent -RNA polymerase inhibitor), several combinations of lopinavir/ritonavir are thereupon being investigated [62, 63]. Besides, Camostat-mesylate, a serine protease inhibitor, restricts access to the cells of SARS-CoV-2 and may demonstrate to be a potential treatment option. [57, 64]. Darunavir/cobicistat (HIV-1 Protease Inhibitor and Cytochrome P450 Inhibitor) is being investigated either for monotherapy or in combination with lopinavir / ritonavir and thymosin α1, which is an immunomodulator [65]. Immunoenhancers such as interferons (recombinant cytokines with antiviral properties), Methylprednisolone (Synthetic corticosteroid), and
cyclosporine A (immunosuppressive agent) may be appropriate as a monotherapy or in conjunction against the SARS-CoV-2 infection [65]. Meanwhile, there is an ongoing study of camrelizumab, which is a humanized monoclonal antibody (mAb) in combination with thymosin to treat severe pneumonia associated with lymphocytopenia in COVID-19 infection [66].

8. VACCINE DEVELOPMENT

Vaccines are crucial as they stimulate the immune system of an individual to defend against potential infection. Until now, vaccines to prevent respiratory infections against nCoV have not been approved for human use. The purpose of vaccine candidates is to induce antibodies that neutralize against the viral spike protein and to prevent uptake via the human ACE2 receptor. As of June, there are about 161 COVID-19 vaccine candidates in various stages of development. We have summarized the vaccine candidates that are under clinical stages in Table 3. It includes traditional recombinant protein, replicating and nonreplicating viral vectors, and nucleic acid DNA and mRNA approaches [67, 68]. To summarize, the time it takes for the vaccines to enter the market depends on the safety and effectiveness in the clinical stages.

CONCLUSION

Natural disasters bring people together but epidemics and outbreaks split them apart. The SARS-CoV-2 is another CoV that leads to a pandemic since it was not timely controlled. The world is witnessing its alarming impact and the number of infected cases to date indicates a very rapid and
Table 3. Summary of vaccine candidates for COVID-19 [69, 70].

| Platform                      | Vaccine Description                                                                 | Phase  | Developer                                                                                                                                 |
|-------------------------------|-------------------------------------------------------------------------------------|--------|------------------------------------------------------------------------------------------------------------------------------------------|
| DNA-based                     | INO-4800: DNA plasmid vaccine with electroporation                                  | Phase I| Inovio Pharmaceuticals/Beijing Advaccine Biotechnology/VGXII Inc./ Richter-Helm BioLogics/Ology Bioservices                                |
| Inactivated virus             | Inactivated                                                                         | Phase I| Institute of Medical Biology, Chinese Academy of Medical Sciences                                                                      |
| Non-replicating viral vector  | AZD 1222 (ChAdOx1)                                                                  | Phase I| Consortium of the Jenner Institute, Oxford Biomedica, University of Oxford, Vaccines Manufacturing and Innovation Centre, Pall Life Sciences, Cobra Biologics, HalixBV, Advent s.r.l., Merck KGaA, the Serum Institute, Vaccitech, and AstraZeneca |
| Protein subunit               | Protein subunit; NVX-CoV2373; Full-length recombinant SARS COV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M | Phase I| Novavax/ Emergent BioSolutions/ Praha Vaccines/Serum Institute of India/ AGC Biologics                                                |
| RNA-based                     | BNT162 :3 LNP-mRNAs                                                                 | Phase I| BioNTech/ Fosun Pharma/ Pfizer                                                                                                          |
| Inactivated virus             | Inactivated                                                                         | Phase II| Beijing Institute of Biological Products/ Sinopharm                                                                                 |
| Inactivated virus             | PiCoVacc: Inactivated (inactivated + alum)                                          | Phase II| Sinovac                                                                                                                                  |
| Inactivated virus             | Inactivated                                                                         | Phase II| Wuhan Institute of Biological Products/ Sinopharm                                                                                  |
| Non-replicating viral vector  | Adenovirus Type 5 vector (Ad5-nCoV)                                                 | Phase II| CanSino Biologics/Beijing Institute of Biotechnology/ Canada's National Research Council                                              |
| RNA-based vaccine             | LNP-encapsulated mRNA (mRNA 1273)                                                   | Phase II| Moderna/ NIAID/ Lonza                                                                                                                   |

Efficient transmission globally. Considering the inadequate health systems of most developing countries, emerging disease outbreaks, such as the ongoing COVID-19 epidemic, may eventually cripple healthcare systems to the detriment of primary healthcare needs. Countries are currently putting their interpretation for treating COVID-19 by antiretroviral and antimalarial drugs. The future paradigm may shift the balance towards the development of the vaccine.

**LIST OF ABBREVIATIONS**

| WHO     | = World Health Organization |
| CoV     | = Coronavirus               |
| MERS    | = Middle East Respiratory Syndrome |
| SARs    | = Severe Acute Respiratory Syndrome |
| nCoV    | = Novel coronavirus         |
| HCoVs   | = Human coronaviruses       |
| COVID-19| = Coronavirus disease of 2019 |
| CCDC    | = Chinese Centre for Disease Control and Prevention |
| VRDLs   | = Virus Research and Diagnostic Laboratories |
| ICMR    | = Indian Medical Research Council |
| DCGI    | = Drugs Controller General of India |
| RBM     | = Receptor Binding Motif    |

ACE2 = Angiotensin conversion enzyme2
RBD = Receptor Binding Domain

**CONSENT FOR PUBLICATION**

The authors declare that they agree for the publication of this article.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest, financial or otherwise.

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