Comprehensive study on clinical responses and socioeconomic characteristics of COVID-19 patients during outbreak

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ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SAR‑CoV‑2) causes coronavirus disease 2019 (COVID‑19) and emerged as a new public health crisis. This RNA virus, which has an origin in bats, is phenotypically and genotypically diverse. The source of transmission is by direct inhalation or contact with infected droplets or indirect through fomites. The disease shows an average incubation period of 2 to 14 days. The general symptoms include fever, cough, sore throat, breathlessness, fatigue, and malaise, although in a few it is found to be asymptomatic. The immune response shows variation from individual to individual, which varies from pneumonia, chest pain, acute respiratory distress syndrome, and multiorgan failure leading to death. The cytokine and chemokine responses play a major role in the severity of the infection. Laboratory diagnosis is done by molecular investigations. The socioeconomic conditions of individuals also play a role in disease manifestation. Treatment is supportive with symptomatic management. Preventive measures include social distancing, use of face masks, and contact tracing. This review will present a general overview of coronavirus and describe the clinical and socioeconomic features of the COVID‑19 patients. It will also introduce comprehensive data of symptomatic and asymptomatic patients among different Asian and Western countries during the current pandemic. Furthermore, it also focuses on the most up-to-date information on effective management and prevention of COVID‑19.

Keywords: Clinical features, coronavirus, COVID‑19, SARS‑CoV‑2, socioeconomic status

Introduction

The World Health Organization (WHO) alerted the Chinese health authorities because several cases of pneumonia that were of unknown etiology originated from the Wuhan city in Hubei Province of Central China on December 31, 2019. A novel coronavirus was identified by the WHO on January 7, 2020, from the throat swab sample of a patient. This pathogen was later named severe acute respiratory syndrome coronavirus 2 (SARS‑CoV‑2) by the coronavirus study group, and the disease was named coronavirus disease 2019 (COVID‑19) by the WHO. China reported 30,7700 confirmed cases and 12,167 suspected cases in January 2020. The WHO has announced the outbreaks of SARS‑CoV‑2 as a Public Health Emergency of International Concern on March 11, 2020. Up to January 19, 2021, around 93,805,610 confirmed cases and 2,026,000 deaths have been reported globally.

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have been reported due to COVID-19 worldwide. The first case of COVID-19 in India was reported on January 30, 2020, in a student who had traveled from Wuhan, China. Currently, India has reached the second position in the list of COVID-19-affected countries, territories, and regions, including 10,571,770 confirmed cases and 152,415 deaths.4

This is the third virus of the corona family that emerged among humans in the past two decades. The first two coronaviruses caused severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle Eastern respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012.5 From the beginning of the COVID 19 pandemic, the Indian government is continuously making a number of interventions such as travel restrictions on international and national passengers, directives on testing and patients care management strategies, self-quarantine measures, and so on.

Although some literature provide insight into some basic information about the demographical and clinical features of the COVID-19 cases in different regions of India and also in other countries, there are disparities in terms of severity of the disease, age of the patients, source of infection, and clinical outcomes. Yet previous studies could not provide comprehensive data, together or alone. In India, there is a lack of comprehensive epidemiological information such as sociodemographic features, comorbidities, clinical presentations, and responses of COVID-19 patients. So, in this framework, the present review tries to summarize the current understanding of COVID-19, including causative agents, the pathogenesis of the disease, immune response, and comprehensive data about socioeconomic status (SES) and clinical presentation.

**Materials and Methods**

We performed a literature search in the Web of Science, PubMed, and Google Scholar using keywords limited to titles and abstracts. The search strategy used in PubMed, Google Scholar, and Web of science was as follows: “SARS-CoV-2,” “Origin of SARS-CoV-2,” “COVID-19 outbreak,” “Clinical sign and Pathogenesis,” “Symptomatic and Asymptomatic,” “Epidemiology,” “Socioeconomic status,” “Treatment and Prevention,” and “Vaccine.” The data were retrieved from published research articles along with national and international websites that contained detailed information throughout the COVID-19 outbreak (December 2019 to January 2021). The searched websites include the WHO, the Centers for Disease Control and Prevention (CDC), the Integrated Disease Surveillance Program, the World Meters, the Indian Council of Medical Research, and the Ministry of Health and Family Welfare, India.

**Virus classification and origin**

SARS-CoV-2 belongs to the family Coronaviridae, subfamily Coronavirinae and, order Nidovirales. Coronavirus is further subdivided into four genera: (1) Alpha coronavirus containing the human coronavirus HCoV-229E and HCoV-NL63; (2) Beta coronavirus including HCoV-OC43, SARS-HCoV, HCoV-HKU1, and MERS-CoV; (3) Gamma coronavirus including viruses of whales and birds; and (4) Delta coronavirus that includes those viruses that are isolated from animals (pigs and birds).6

SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA (+ssRNA) virus. The typical structure of the SARS-CoV-2 genome is presented like coronaviruses and encloses 10 open reading frames (ORFs). The ORFs, specific to SARS-CoV-2 on one third of the genome, encodes four main structural proteins: Envelope, membrane, spike, and nucleocapsid proteins [Figure 1].7,8

**Pathogenesis and immune response**

The transmission of infection is found to be through respiratory droplets, which occur mainly by coughing or sneezing in public. Another indirect mode of transmission occurs through fomites on large scale. It has been seen that SARS-CoV persists up to 96 hours on surfaces.9 High species specificity is shown by the Beta coronavirus and other members of its family. Their tissue tropism, host range, and pathogenicity are significantly altered by minute genetic changes.10 The envelope spike protein receptor-binding domain of SARS-CoV-2 is similar in structure to that of SARS-CoV, although the variation of amino acids can be found at some key residues.11 Spike protein has been reported as a significant determinant of virus entry into the host cells. The entry of SARS-CoV-2 into cells was initially identified to be accomplished by direct membrane fusion between the virus and the plasma membrane.5

Prominent clinical features shown by COVID-19 patients are rhinorrhea, sneezing, and sore throat. This virus shows a greater preference for infecting the lower respiratory tract than the upper respiratory tract due to the increased expression of ACE-2 (angiotensin-converting enzyme 2) receptors.12 Thus, it is essential to study the host adaptation, viral evolution, infectivity, transmissibility, and pathogenicity of this disease. ACE-2 receptor facilitates SARS-CoV to contaminate the epithelium airway and alveolar type 2 (AT2) pneumocytes, pulmonary cells that synthesize pulmonary surfactant. In response to SARS-CoV infections, the type I interferon (IFN)
system of the host induces the expression of IFN-stimulated genes to inhibit viral replication. SARS-CoV severity depends on the expression of ACE-2 receptors in type II pneumocyte cells of the host. Other receptors to which they can bind are Ezrin, CD26, and cyclophilins. Neprilysin, prolyl carboxypeptidase, and prolyl endopeptidase are enzymes capable of hydrolyzing angiotensin (Ang) 1 or Ang 1–9 due to which severity of COVID-19 varies. Activated host megakaryocytes of the lung lead to platelet fibrin deposition, aggregation, and clot formation, which are involved with the pathophysiology of the COVID-19 patients. The inflammatory mediators produced as a result of infection with SARS-CoV are, for example, interleukin (IL)-1, IL-6, IL-12, interferon-gamma (IFN-γ)-induced protein 10 (IP-10), macrophage inflammatory proteins 1A and monocyte chemo-attractant protein–1 (MCP-1), which are associated with pulmonary inflammation and severe lung damage [Figure 2]. Few studies also report that patients infected with SARS-CoV-2 are reported to have higher plasma levels of proinflammatory cytokines, including IL-1, IL-2, IL-7, tumor necrosis factor–alpha (TNF-α), granulocyte colony-stimulating factor (G-CSF), and MCP-1, than healthy adults that can be used as inflammatory markers. Other interesting findings have been found that higher levels of G-CSF, IP-10, MCP-1, and TNF-α are found in intensive care unit (ICU) patients than in non-ICU patients. This suggests that a cytokine storm might be related to the disease severity. Most studies have demonstrated that males were more likely to be hospitalized and die from COVID-19 as compared with females; thus, higher rates of mortality in the male population show that males were more severely infected as compared with females. The studies also suggested that self-isolation is critical for the prevention of the spread of the COVID-19 pandemic; therefore, strategies of contact tracing are essential to combat this disease.

Viral transmission and clinical features

The WHO has classified transmissions of COVID-19 infections into three forms as scattered, clustered, and community-based.

The routes of transmission are sneezing, coughing, and contact transmission via oral, nasal, and eye mucosa of the 2019 novel coronavirus. A distance of 6 feet is emphasized to protect against the spread of the disease, although this is not enough as microbes in droplets <5 µm in diameter can stay in the air for a longer time and can be transmitted to others over distances of more than 1 m. Surfaces and objects contaminated by an infected person are also one of the indirect modes of transmission among individuals.

The regulatory bodies such as the WHO and the Indian Council of Medical Research (ICMR) issued guidelines for clinical related diagnosis to COVID-19 infection: (1) Suspected cases of COVID-19 are identified based on (a) severe acute respiratory infections along with a history of travel or (b) a patient with an acute respiratory illness 14 days before contact with a confirmed or probable case of SARS-CoV-2 infection and has worked in a healthcare facility where COVID-19 positive cases are being treated. A probable case is defined as a person tested for SARS-CoV-2 and the result is inconclusive or whose pan-coronavirus panel is being tested positive. (2) A confirmed case is defined as a person with a laboratory report of SARS-CoV-2 infection. The CDC guidelines for the SARS-CoV-2 testing recommend the collection of specimens from the upper respiratory tract (nasopharyngeal and oropharyngeal swabs) and the lower respiratory tract (sputum, tracheal aspirate, and or bronchoalveolar lavage) of the patient, if possible. In each country, the tests are performed in laboratories designated by the government.

The average incubation period of the COVID-19 virus is reported as 5 to 6 days. After the onset of the symptoms, the average period of the disease is about 14 days. The presentation of the symptoms of the disease is found to be more severe in pediatrics and geriatrics age groups as compared with the younger age group without any immunocompromised condition. The latency period of the SARS-CoV-2 can also be extended up to 24 days based on recent large-scale epidemiological studies. Reported illnesses in patients have ranged from no symptoms to being severely ill and dying. The main clinical manifestations have been observed as fever, cough, fatigue, and dyspnea. However, the clinical features between severely and mild affected COVID-19 patients have not yet been well described to date. The SARS-CoV-2 presents worse disease progression and contagious infectiousness in asymptomatic conditions.

A meta-analysis report on 4,499 COVID-19 patients in Africa showed that positivity in men was approximately 68%. The common symptoms were fever (42.8%), cough (33.3%), breathlessness (16.8%), and headache (11.3%), whereas diarrhea (7.5%) and rhinorrhea (9.4%) were the least common symptoms encountered. A study suggested about higher susceptibility of COVID-19 in males could be because of ACE-2 expression pattern.

In a study cohort (n = 3,745) with confirmed diagnosis of SARS-CoV-2 infection, 60% patients (n = 2,245) were
symptomatic and 40% patients (n = 1,500) were asymptomatic. The most common presenting symptoms were cough, breathlessness, and sore throat. Cough along with breathlessness (24.1%) was the most common combination of symptoms followed by fever with cough (22.7%). Comorbidities such as diabetes mellitus and chronic diseases of the lungs, heart, and kidneys were found to be common in the symptomatic group. Some studies with their clinical outcomes conducted in India and abroad are summarized in Table 1.

The European and American regions have been affected severely by the virus other regions of the world. Till January 2021, the Integrated Disease Surveillance Programme (IDSP) of India exclusively reported that about 80% of the COVID-19 patients were asymptomatic. The younger age group population (20–40 years) often tend to be asymptomatic and are, hence, the drivers of the disease. It has been found that the mortality rate is higher among middle-aged and elderly cases as compared with young healthy individuals. A large cohort study was done in India by Kumar et al. which showed that approximately 91% of cases were asymptomatic, whereas only 9% were symptomatic. Ultimately, it has been more challenging for clinicians, health workers, and policymakers. Thus, an in-depth study is required to understand the behavior and role of asymptomatic cases in the COVID-19 pandemic.

**SES and COVID-19 pandemic**

Developed countries such as the USA, France, UK, Germany, Italy, Spain, and China have higher fatality rates. The spread of SARS-CoV-2 in poor people would cause a tremendous burden on the health care systems. The socioeconomic impact has put remarkable pressure on the individual, family, and community levels of each country.

The current population of India is estimated as 1,380,004,385 with a population density of 464 per square kilometer, and India is ranked second in the world in terms of both total population and population density. This demographic status of India raises the concern of the rate of spread and the transmission of the COVID-19 disease. Although the government of India released the funds for the medical equipment and supplies, it was insufficient due to the rapid increase in demand throughout the country. So, COVID-19 could have a significant influence on the long-term economic effects in India. SES plays a significant role in the COVID-19 pandemic either directly or indirectly via occupation, living conditions, and health-related behaviors of the patients. Moreover, the morbidity and mortality of COVID-19 also cause an economic burden on the family of the survivors.

The strength of the immune response of patients depends on genetic predispositions, epigenetics, and lifestyle. Factors such as overcrowded houses, lack of food and nutrition, and the necessity to continue working may prohibit individuals in poor, underserved communities from self-isolation and social distancing. The severity of COVID-19 symptoms is not well-known about SES, which needs further scrutiny and investigation.

Shi et al. found that among the 484 COVID-19 patients in the Zhejiang Province of China, more severe cases were found in agricultural workers and self-employed persons. Similarly, Khan et al’s report on 172 COVID-19 patients of Scotland

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**Table 1: List of previous studies on COVID-19 patients highlighting their clinical features**

| Study          | Country  | Sample number (n) | Clinical Conditions | Symptoms                                      | Comorbidities                      |
|---------------|----------|------------------|---------------------|-----------------------------------------------|-----------------------------------|
| Gupta et al.  | India    | 21               | Asymptomatic (n=9)  | Cough, fever, sore throat, breathlessness,    | Hypertension, diabetes            |
|               |          |                  | Symptomatic (n=12) | headache                                      |                                   |
| Tambe et al.  | India    | 197              | Asymptomatic (n=45) | Cough, fever, headache, breathlessness,       | Hypertension, diabetes            |
|               |          |                  | Symptomatic (n=152)| chest pain, nausea, diarrhea                  |                                   |
| Prakash et al.| India    | 17               | Asymptomatic (n=7) | Cough, fever, breathlessness                  | Hypertension, diabetes, COPD      |
|               |          |                  | Symptomatic (n=10) |                                               |                                   |
| Bhandari et al.| India    | 21               | Asymptomatic (n=7) | Cough, fever, headache, myalgia, dyspnea      | Hypertension, diabetes, hypothyroidis, CAD, chronic kidney illness |
|               |          |                  | Symptomatic (n=14) |                                               |                                   |
| Joshi et al.  | Nepal    | 4                | Asymptomatic (n=2) | Cough, fever                                  | Chronic rhinitis                  |
|               |          |                  | Symptomatic (n=2)  |                                               |                                   |
| Khan et al.   | Pakistan | 121              | Asymptomatic (n=121)| Cough, fever, breathlessness, nausea,         | Hypertension, diabetes, CAD, COPD, HIV, HCV, HBV, tumor |
|               |          |                  | Symptomatic (n=121)| diarrea, sore throat                           |                                   |
| Mohan et al.  | India    | 144              | Asymptomatic (n=64) | Fever, throat sore, cough, sputum, dyspnea,   | Hypertension, diabetes, hypothyroidism, CAD, Parkinsonism, COPD, tuberculosis |
|               |          |                  | Symptomatic (n=80) | fatigue, diarrheaa, headache, earache, myalgia|                                   |
| Wang et al.   | China    | 107              | Asymptomatic (n=107)| Fever, cough, fatigue, dyspnea, anorexia,     | Hypertension, CAD, diabetes        |
|               |          |                  | Symptomatic (n=107)| myalgia                                       |                                   |
| Aggarwal et al.| USA      | 16               | Asymptomatic (n=52) | Fever, cough, dyspnea, chest pain, nausea,    | Obesity, Hypertension, Diabetes,  |
|               |          |                  | Symptomatic (n=32) | fatigue, headache, arthralgia, anemia,        | CAD, COPD, chronic kidney disease, malignancy |
|               |          |                  |                     | dysgeusia, anosmia                           |                                   |
| Buckner et al.| USA      | 105              | Asymptomatic (n=41) | Fever, cough, dyspnea, fatigue, diarrheaa,    | Hypertension, obesity, diabetes,  |
|               |          |                  | Symptomatic (n=66) | sore throat, nausea                           | COPD, chronic kidney disease, sleep apnea, cancer |

*COVID-19*: coronavirus disease 2019, COPD: chronic obstructive pulmonary disease, CAD: coronary artery disease, HIV: human immunodeficiency virus, HCV: hepatitis C virus, HBV: hepatitis B virus
illustrated that the lower socioeconomic group was significantly associated with COVID-19 infection. It may due to the fact that lower socioeconomic groups have more risks of comorbidities. It has been reviewed that middle and lower socioeconomic groups of people are more exposed to job stress and unemployment, due to which the infection is more marked in these age groups. This may lead to various organ involvement, marked immune responses, and release of inflammatory cytokines leading to increased risk for cardiovascular disease. Therefore, strategies to avoid the socioeconomic and demographic discrepancies should be considered at the state and federal levels in the fight against COVID-19.

Jia et al. (2020) analyzed the socioeconomic characteristics of COVID-19 positive cases. A major proportion of the cases was found to be employees (45.5%), followed by retirees (18.2%). A recent study of India reported that low SES was associated with a higher incidence of COVID-19 infections, whereas the authors did not analyze SES as a risk factor for morbidity and mortality of COVID-19.

The pandemic has an alarming effect on individual emotional and social health, which has led to social loss and disparity of the person affected. Health care systems have an important role in psychosocial monitoring along with providing emotional and moral support to the patients. Currently, telemedicine is being offered to psychosocial services delivered in primary care settings. In this context, the assessment queries include exposures to infected sources, contact with infected family members, death, and social distancing. The psychosocial consequences of infection include anxiety, insomnia, depression, and domestic violence.

Treatment
There is no specific antiviral treatment for COVID-19 infection; only preventive measures such as isolation and supportive care that includes oxygen therapy, fluid management, and antibiotics treatment for secondary bacterial infections are recommended. Antiviral drugs such as oseltamivir, combined with empirical antibiotic treatment, have also been used to treat COVID-19 patients. Remdesivir, initially developed for the Ebola virus, has been used to treat imported COVID-19 cases in the USA, although it was not found to be effective. A brief report stated that a combination of lopinavir/ritonavir, and arbidol along with adjunctive agents such as vitamin D, zinc, azithromycin, nitric oxide, ascorbic acid, corticosteroids, and IL-6 antagonists are beneficial for the COVID-19 treatment. As seen in many cases and supported by several other studies, the viral load reaches its peak around the time of symptom onset. A combination of antiviral drugs and adjunctive agents may suppress the virus load and can be effective in lowering the severity of the disease. Few herbal agents such as ginseng (Panax ginseng) regulate the activity of immune cells. Ginger (Zingiber officinale) has shown antiapoptotic, antitumorogenic, anti-inflammatory, antihyperglycemic, antioxidant, and analgesic properties, and is used for the cure of this disease. Similarly, garlic (Allium sativum) and echinacea extract (Echinacea purpurea) have also been found to have antimicrobial and antioxidant properties and are hence used to improve the immune system.

Prevention
Suspected cases presenting at the health care facilities with symptoms of respiratory infections must wear a face mask to control the spread of the COVID-19 infection. These patients should be placed in a separate room with a distance of 2 meters between the beds, and the rooms should be fully ventilated. Hospitalized COVID-19 patients should be placed in a single room with six air changes per hour having negative air pressure. The exhausted air should be filtered through high-efficiency particulate air filters, and the medical personnel entering the room should wear personal protective equipment, gloves, gown, disposable N95 mask, and face shields.

Isolating the infected people is the primary measure to interrupt the transmission of this virus in the community. Moreover, awareness of the general public about unusual symptoms such as shortness of breath and chronic cough is essential so that they could seek medical care and advice for early and easy detection of the virus. Community transmission can be stopped by avoiding social gatherings, home isolation, and monitoring of the symptomatic individual. Provision of life supports, personal hand hygiene, and face mask must be enforced among the general public.

Recently, two indigenous COVID-19 vaccines have been developed and manufactured by different pharmaceutical companies of India with the collaboration of the National Institute of Virology and the ICIR. These vaccines are developed by using the whole virion-inactivated vero cell–derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects, but they are still capable of developing the immune system and raising a defensive system against the COVID-19 infection.

Conclusion
The current COVID-19 pandemic is an international public health problem. There have been rapid advances in what we know about the pathogen, how it infects cells and causes disease, and the clinical characteristics of the disease. The present report indicates the variable clinical presentation of COVID-19 patients. Asymptomatic condition of patients, despite the SARS-CoV-2 infection, poses a high risk to the population. In symptomatic patients, fever cough, breathlessness, and sore throat were the most common symptoms. Comorbidities such as diabetes, hypertension, and chronic obstructive pulmonary disease were found to be common in symptomatic patients. So, preliminary pathological and radiological investigations of patients and their clinical relation are needed for the early identification of SARS-CoV 2 infection, management of patients, and prevention of widespread community transmission. Due to
rapid transmission, countries around the world should increase attention to disease surveillance systems and scale up country readiness and response operations, including establishing rapid response teams and improving the capacity of the national laboratory system for testing and detection.

**Key points**

1. The first case of COVID-19 in India was reported on January 30, 2020.
2. To summarize the current understanding of COVID-19, including causative agent, the pathogenesis of the disease, immune response, and SES.
3. SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA (+SS RNA) virus, which encloses 10 ORFs.
4. This virus shows a greater preference for affecting the lower respiratory tract in comparison with the upper respiratory tract due to increased expression of ACE-2 receptor.
5. The inflammatory mediators produced as a result of infection with SARS-CoV-2 are IL-1, IL-6, IL-12, IFN-γ, IP-10, MIP1α, and MCP-1, associated with pulmonary inflammation and severe lung damage.
6. Cytokine storm is related to the disease severity, more common in ICU patients than in non-ICU patients.
7. The route of transmission is sneezing, coughing, and contact transmission via oral, nasal, and eye mucosa.
8. The average incubation period of COVID-19 is reported to be 5 to 6 days, and the period of the disease is about 14 days. The main clinical features are fever, cough, fatigue, and dyspnea.
9. Strength of the immune response of patients depends on genetic predispositions, epigenetics, and lifestyle.
10. Preventive measures such as isolation and supportive care including oxygen therapy, fluid management, and antibiotic treatment for secondary bacterial infections are recommended.

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**Conflicts of interest**

There are no conflicts of interest.

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