

SARS-CoV-2 / COVID-19 and its Transmission, Prevention, Treatment and Control - An Update

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Abstract

Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Virus-2 (SARS-CoV-2), pandemic has caused huge panic, havoc and global threats worldwide. The origin of this virus has been linked to animals, intermediate host is still to be identified, and studies are being carried out that how it got transmitted to humans and acquired rapid human-to-human transmission. Within a short time period of only 05 months, SARS-CoV-2 has spread to 213 countries, and till 28th May, 2020, nearly 5.8 million confirmed cases have been reported while taking lives of 0.36 million persons. Seeing the current situation of rapid increase in COVID-19 cases daily in many countries, this seems to be the deadliest pandemic after the 1918 Spanish Flu. There is currently no specific effective treatment for COVID-19 and also in absence of vaccine the radical cure of the disease is far away. Researchers are pacing high to design and develop effective vaccines, drugs and therapeutics to counter COVID-19, however such efforts, clinical trials, necessary approvals and then to reach the level of bulk production of many millions of doses may still take much time. Prevention and control of COVID-19 outbreaks requires an evidence-based, multi-factorial and effective mitigation strategy to be adopted. The current review discusses on the research advancements, challenges and opportunities in COVID 19 management with a focus on its transmission, prevention, treatment and control.

Keywords: COVID-19, SARS-CoV-2, transmission, prevention, treatment, control

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(Received: April 24, 2020; accepted: May 28, 2020)

Citation: Sharma P, Tripathi S, Patel SK, Dhama K, Chandra R. SARS-CoV-2 / COVID-19 and its Transmission, Prevention, Treatment and Control - An Update. *J Pure Appl Microbiol.* 2020;14(suppl 1):945-956. doi: 10.22207/JPAM.14.SPL1.32

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INTRODUCTION

A novel coronavirus named as Severe Acute Respiratory Syndrome Virus-2 (SARS-CoV-2), the causative agent of Coronavirus Disease 2019 (COVID-19), emerged in Wuhan, China in December month of the last year (2019). It attained the status of public health emergency of international concern on January 30, 2020, and later on March 11, 2020 was declared as a global pandemic by World Health Organization¹. The International Committee on Taxonomy of Viruses (ICTV) recognized the virus as SARS-CoV-2 (earlier known as nCoV-2019) and the disease was named as coronavirus disease 2019 (COVID-19) by WHO². The virus has now caused huge panic and very high global threats to the lives of mass population across the globe. The global risk of COVID-19 is increasing progressively for the general public and considered to be very high for the communities with identified risk factors. The virus appears to be highly infectious and has spread rapidly throughout the globe. A meeting was held on this issue on 30th January 2020 under the International Health Regulations (IHR, 2005) and WHO declared the outbreak as Public Health Emergency of International Concern (PHEIC) because it had spread to 18 countries with four countries reporting human-to-human transmission. Currently, nearly 06 million individuals from 213 countries and territories are affected from the SARS-CoV-2 infection with over 0.35 million deaths worldwide³. Presently, the USA, Brazil, Russia, Spain, UK, Italy, France, Germany, Turkey and India are among the list of top 10 COVID-19 affected countries, which overload the healthcare system due to high patient burdens needing intensive care and treatment. As on 28th May, 2020, 4,534 deaths out of a total of 1,58,086 confirmed cases of COVID-19 have been reported from India⁴.

Moreover, earlier coronaviruses (CoVs) viz. Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-Cov) also induced lethal outbreaks but the currently ongoing SARS-CoV-2 pandemic is the deadliest among all the zoonotic CoVs. On 20 January 2020, China announced the disease as a second-class infectious disease, but followed prevention and control strategies for the first-class infectious disease, the most risky

category of infectious diseases⁵. The COVID-19 was first reported as pneumonia of unknown origin in China and then spread like wildfire to the rest of the world, posing a noteworthy global threat to the public health globally^{6,7}. Presently, there is no effective vaccine or treatment option available for COVID-19, and for this purpose high efforts are continuously being made by researchers from many countries.

In particular, reports showed that 2 % population are healthy carriers of CoVs and these viruses contribute for 5 to 10 % of acute respiratory infections. A total of seven CoVs have been reported to infect human's viz., HCoV-229E, HCoV-NL63, HCoV-HKU1 and HCoV-OC43, capable of causing mild respiratory symptoms alike to that of common cold, while SARS-CoV-2, SARS-CoV and MERS-CoV have been associated with fatal infections^{8,9}. SARS-CoV (2003) has previously infected 8096 people with 774 deaths at a case fatality rate of 9.6% around the world, although the rate of survival is higher among the COVID-19 patients but the rate of infection is growing exponentially which may have a larger impact. Even though COVID-19 is spreading rapidly through airborne route, air disinfection of towns and communities was not found to be effective enough in disease control. This review presents current knowledge and advances on SARS-CoV-2 / COVID-19 management and specifically highlighting its transmission, prevention and control strategies.

Characteristics of SARS-CoV-2

Coronaviruses (CoVs) belong to the family *Coronaviridae* in the order of Nidovirales. The SARS-CoV-2 represents crown-like spikes on the envelope of the virus; hence named coronavirus¹⁰. Coronavirinae consists of four main sub-groupings / genera, Alpha-, Beta-, Gamma- and Delta-coronavirus, and that the first two host human infecting viruses (Human Coronavirus, HCoV): HCoV-229E and HCoV-NL63 (alpha coronavirus) and HCoV-HKU1, HCoV-OC43, Middle East coronavirus respiratory syndrome (MERS-CoV), extreme acute coronavirus respiratory syndrome (SARS-CoV) (beta coronavirus)^{11,12}. The CoVs including the SARS-CoV-2 have a non-segmented, single stranded, positive sense RNA genome of around 30 kb^{11,13} (Fig. 1). The SARS-CoV-2 is a member of the sub-family *Orthocoronavirinae*

under the family *Coronaviridae*¹⁴. On the basis of molecular characterization, the virus has been reported to be a new betacoronavirus that belongs to the subgenus *Sarbecovirus*¹⁴. An overall 80% identity between SARS-CoV-2 and SARS-CoV along with 89% identity with two bat SARS related CoVs (ZC45 and ZXC21) has been reported at nucleotide level^{13, 15}. The structural proteins of CoVs are encoded by four structural genes, including spike (S), envelope (E), membrane (M) and nucleocapsid (N) genes. The S protein makes the spike on the virion surface and is responsible for the binding with host cell receptor^{16,17,13}. The SARS-CoV-2 has a typical coronavirus structure with S protein and also expresses other polyproteins, nucleoproteins and membrane proteins including RNA polymerase, 3chymotrypsin-like protease, papain-like protease, helicase, glycoprotein and accessory proteins¹⁸.

The entire mechanism of SARS-CoV-2 pathogenicity, from entry, attachment to replication, is presented in Fig. 1. Viruses use the large network of host cell signalling pathways to facilitate their replication and spread (propagation). Each encoded viral protein has a distinct structural role and also get associated in other mechanisms of the replication cycle. Unlike other major structural proteins, N protein functions mainly to bind to CoV RNA genome, rendering it a nucleocapsid¹⁹. Moreover, in virus-infected cells, N protein of the CoVs may be clustered either to the cytoplasm alone or to the cytoplasm and nucleolus. The M protein is the most copious structural protein that determines the structure of the viral envelope²⁰. The endoplasmic reticulum (ER) can maintain a high protein content without getting weighed down. Furthermore, once the ER folding and dealing out protein capacity is overloaded, the unfolded proteins swiftly build up in lumen and ER stress reaction is activated²¹. This is also known to be the main organizer of the coronavirus group, communicating with all other large structural corona viral proteins. The ORF1ab as the largest gene in SARS-CoV-2 encodes pp1ab and 15 nsps. The ORF1a gene encodes pp1a protein, contains 10 nsps²². SARS-CoV-2 also utilizes the same ACE2 (angiotensin-converting enzyme 2) cell receptor and host cell entry mechanism as used by SARS-CoV^{15, 23}. The single mutation of N501 T in SARS-CoV-2 Spike protein might have notably improved

its binding affinity to ACE2 receptor²⁴.

COVID-19: The Disease

Individuals diagnosed with SARS-CoV-2 show symptoms of different classes from fever or mild cough to pneumonia and severe involvement of various organ dysfunctions with a mortality rate from 2% to 4%⁹. In general, the SARS-CoV-2 causes fever, dry cough, generalized weakness, respiratory distress, muscle ache, rhinorrhoea, pleuritic chest pain and to some extent headache, nausea, vomition, haemoptysis and diarrhoea^{25,13,7}. A range of sickness in children has been reported from SARS-CoV-2 infection²⁶. SARS-CoV-2 has also been implicated in causing damaging effects on the central nervous system (CNS) as observed while investigating viral encephalitis cases^{27,28}. Systemic Inflammatory Response Syndrome (SIRS) may well be unusually triggered in severe pneumonia caused by CoV disease, although early anti-inflammatory treatments can effectively prevent immune damage and reduce the impact of damage to the nervous system^{29,30}. Moreover, the rampant inflammation in response to SARS-CoV-2 infection resulted into cytokine storm associated with release of pro-inflammatory cytokines and chemokines like IFN- γ , IL-1 β , IP-10, MCP-1, TNF- α , G-CSF, MCP-1, IP-10, and MIP-1A, which is reported to severely damage the pulmonary tissues and leads to death in severe COVID-19^{31,32}. The blood profile of the COVID-19 affected individuals exhibits leukopenia, lymphopenia, thrombocytopenia, RNAemia along with increased hypersensitive troponin I and aspartate aminotransferase levels⁷. In sub-regions of Italy, SARS-CoV-2 infection got more widely spread in elderly people. The associated clinical presentation include fever, cough, malaise and acute respiratory distress syndrome (ARDS), which is reported to be a major cause of increased mortality among these immunocompromised patients^{13,33,34}.

Transmission and Spread

According to the WHO, viral diseases will go on emerging and pose grave public health concerns globally. Many viral epidemics in the 21st Century, including SARS in 2002 to 2003, Influenza (H1N1) in 2009 and MERS in 2012, and recent episodes of Ebola, Zika, Nipah have been reported³⁵. The role animals and zoonotic links have been implicated in the origin of SARS-

Environmental circumstances like temperature appear to have an effect on the ability of CoV to survive in water. Further studies are required to examine the persistence of CoV in water in relation to climatic and seasonal conditions⁴⁹. SARS-CoV-2 has been reported to be found in patient's fecal and anal swabs and the risk of fecal-oral transmission including water-borne transmission need to be studied and explained⁴⁹. SARS-CoV-2 viral RNA has been detected in wastewater of hospital isolation wards and sewage water, which has high public health concerns, and therefore appropriate surveillance and treatment of wastewater need to be followed to avoid mass transmission and spread of COVID-19⁵⁰⁻⁵². Hence to minimize the possibility of false negative results during the preliminary screening, faecal samples must be tested as a complementary method for initial diagnosis of COVID-19. In this context, COVID-19 confirmed cases should only be declared as negative when oropharyngeal samples along with faecal samples were tested negative because prolonged viral shedding was reported even in cured patients suggesting the potential possibility of unintentional fecal-oral transmission⁵³. Moreover, the collection of faecal sample is a non-invasive method and can be performed easily by the patient itself preventing the possibility of nosocomial transmission too⁵⁴. Data analysis relevant to the spread of SARS-CoV-2 in China appears to suggest that close communication between individuals is important for transmission. In addition, the distribution is mainly limited to family members, health professionals as well as other close contacts. Previously reported histopathological information on the lungs of 02 patients subjected to lung lobectomy for adenocarcinoma, revealed an infection at the time of surgery, supporting the phenomenon of nosocomial infection⁵⁵.

There have been studies of new-born babies tested positive for COVID-19 after birth from mothers who have also been tested positive for COVID-19⁵⁶. Wei et al. (2020)⁵⁷ reported that children of all the ages, such as new-born babies and young children may also be infected. Furthermore, having COVID-19 while pregnancy may still have an impact on the fetal outcome, including fetal distress, potential preterm birth and breathing difficulties⁵⁸.

Necessary risk assessment of the pandemic

Increased duration of hospitalization, ICU bed occupation and ventilators requirements by COVID-19 patients is a major issue of concern for the countries facing the pandemic. We have learned more about how COVID-19 affects people as the pandemic is advancing. The older people suffering from chronic illnesses such as diabetes, heart disease, are at higher risk of severe COVID-19 problems⁵⁹. This virus also severely affects children below 5 years of age having compromised immune system. We know that people of any age may be infected with the virus but the mortality is very high in people with comorbidities especially of older age group. In absence of an effective radical cure, large scale testing, lock down and social distancing is the only ray of hope till date. People might also be infected by touching surfaces infected with the virus followed by touching their face, eyes, nose and mouth without taking the necessary preventive steps.

Latest reports of COVID-19 infectious diseases demonstrated that the both community-dwelling senior citizens as along with those in assisted living facilities, nursing homes and other congregated living facilities would be at greater risk of the SARS-CoV-2 infection⁶⁰. Moreover, emergency concerns which need to be discussed include whether pregnant women with COVID-19 diagnosed pneumonia can experience distinct symptoms from non-pregnant adults, and are also much more likely to die from infection or undergo preterm labour, and COVID-19 could spread vertically and cause risks to the foetus and neonate⁶¹.

People at high-risk are as follows:

- Living with someone who has contracted the virus.
- Providing home treatment to someone who has contracted the virus.
- Maintain distance from person who has contracted the virus and also some appropriate distance in home.
- Immunocompromised, having other illnesses, elderly and young children.
- Consult a doctor if symptoms of COVID-19 seems to be started.
- Do not delay in getting medical treatment besides your underlying illnesses condition.
- Serious heart diseases, like heart problems,

coronary artery disease, congenital heart disease, lung cancer, and pulmonary hypertension, can put patients at greater risk for severe COVID-19.

- Older people (65 years) are at greater risk of severe illness and death from COVID-19.
- Young children are at greater risks of acquiring severe COVID-19.
- Some conditions and therapies may cause some people to get a weak immune system, such as cancer treatment, bone marrow or organ transplantation, immune deficiencies, low CD4 cell count in HIV, prolonged use of corticosteroids and other immune disabling drugs, putting at high risk of COVID-19.
- Haemoglobin disturbances like sickle cell disease (SCD) and thalassemia can put patients at greater risk for a severe disease owing to COVID-19.
- Diabetes, like type 1, type 2 or gestational, put patients at greater risk of a serious illness due to COVID-19.
- Chronic lung and kidney disease, including chronic obstructive pulmonary disease (COPD) idiopathic pulmonary fibrosis and cystic fibrosis, could put people at higher risk of COVID-19

Pregnant women are at greater risk owing to scarcity of information regarding possibility of *in-utero* infection of the SARS-CoV-2, therefore a thorough systematic examination of SARS-CoV-2 infected pregnant women and further follow up screening is utmost necessary⁶².

Treatment and control

There is currently no vaccine available for COVID19 and a vaccine may take more than a year to be available widely even after the great efforts were being made by the researchers of different countries in order to develop them. Additionally, considering the rapid pace of vaccine development, one can assume that we are not too far from our goal to develop an effective vaccine against the SARS-CoV-2⁶³. Moreover, some of the signs and symptoms could be treated and early care by a healthcare provider can make the disease less risky. Several potential specific therapies, drugs and medicines are being explored as well as their clinical trials are underway in the search of possible treatment for COVID-19^{64,65}. The

WHO, CDC and FAO have released guidelines and COVID-19 safety measures for common people, physicians, travellers and infectious patients to avoid risk of transmission and spread to a healthy individual⁶⁶⁻⁶⁸. Governments of different nations are advising travellers to defer their tours in order to prevent contact to COVID-19 affected countries, and persons coming back from affected countries are being isolated, quarantined and monitored for health check-ups as well as screened for SARS-CoV-2 so as to avoid further spread to other persons⁶⁹⁻⁷¹. It has been reported that the CoVs may be inactivated on contaminated surfaces or inanimate objects by treatment with biocidal agents, like 62-71% ethanol, 0.5% hydrogen peroxide and 0.1% sodium hypochlorite disinfectants for a minimum period of 1 minute³⁸.

The antiviral therapy commonly used against CoVs globally includes antiviral like ritonavir, ribavirin, lopinavir and interferons or their combination⁷². However, the antivirals like acyclovir, oseltamivir, zanamivir, paramivir, ganciclovir and ribavirin used for the treatment of viral infections are not recommended for COVID-19 treatment⁷³. A combination of ritonavir and lopinavir commonly used for treatment of the human immunodeficiency virus (HIV) showed promising results in case of SARS and MERS but the safety and efficacy of this combination in COVID-19 is being evaluated^{74,75,77,76}. In addition, the ritonavir and lopinavir combination was recommended against SARS-CoV-2 infection in China during the early stages of the pandemic^{77,78}. The remdesivir (A nucleotide analogue) was reported to be administered in Ebola virus patients and has also been proved effective against the coronavirus⁷⁹. Studies have also reported that certain other medications could be used for potential effectiveness in the treatment of COVID-19, such as darunavir, a second generation HIV-1 protease inhibitor. Second is transmembrane type II serine protease (TMSPPS2) inhibitors and BCR-ABL imatinib kinase inhibitor. Imatinib has anti-corona activity mainly as it prevents fusion of virions with the membrane of the endosoma⁸⁰. Favipiravir is a new RNA-dependent sort inhibitor of RNA polymerase (RdRp) in COVID-19⁸¹. Additionally, therapeutics like arbidol (umifenovir), tenofovir disoproxil (TDF), lamivudine (3TC), RNA synthesis inhibitors, hormones and conventional

Chinese capsules viz. Lianhuaqingwen and ShuFengJieDu were also reported to be widely used against SARS-CoV-2 but their efficacy needs to be determined by *in-vivo* and *in vitro* trials⁷⁶.

The chloroquine phosphate (anti-malarial drug) was reported to be the first drug found effective against the SARS-CoV-2 in China⁸². Additionally, the chloroquine was included in the "Guidance for Corona Virus Disease 2019: Chloroquine was used in earlier *in vitro* studies to block a low-micro molar infection of SARS-CoV-2 concentration, with a half-maximum efficiency concentration (EC_{50}) of 1, 13 μ M and half-cytotoxicity concentrations (CC_{50}) greater than 100 μ M⁸³. Due to the easy availability and low cost of the chloroquine and its analogue viz. hydroxychloroquine these drugs may prove crucial to contain the SARS-CoV-2 after proper efficacy and safety evaluation by clinical trials. Moreover, a study also hypothesized the synergistic and consequential effect of hydroxychloroquine and ivermectin for chemoprophylaxis along with clinical care of SARS-CoV-2 infection upon simultaneous administration⁸⁴. Artificial intelligence technology is being exploited to recognize repurposed drugs and medicines having potent prospective in therapeutic application for countering COVID-19⁸⁵. Antibodies-based immunotherapies such as monoclonal antibodies (mAbs), neutralizing antibodies (NAbs), intravenous immunoglobulin (IVIg), and the use of convalescent plasma therapy are also good options which are being explored to counter COVID-19⁸⁶⁻⁸⁸.

The host-directed therapies like glitazones, metformin, fibrates, sartans, atorvastin, nutrient supplements and zinc based supplements along with other drugs with a good safety profile may also be used against SARS-CoV-2 as an alternative treatment option⁸⁹. Studies have so far been demonstrated many agents, such as Western medicines, natural products, traditional Chinese medicines, plants and herbs for use in possible prevention and treatment against COVID-19^{81, 65, 90}. Changes in dietary habits during the epidemic COVID-19 may also be motivated by fear and anxiety⁹¹. Apart from searching for anti-viral drugs and vaccines, choosing appropriate food systems, having balanced foods in regular diets, incorporating herbs and traditional medicines, and sufficient amount of dietary zinc and vitamins A, C,

E, B6 and B12 are essential for the maintenance of better immune function to fight against COVID-19^{92, 65}. Yoga and health exercises are also helpful to maintain the biological function and enhance the immunity.

In the current scenario of lack of any vaccine or drug, adopting early and rapid diagnosis, following appropriate isolation and quarantine policies, enhancing viral surveillance and monitoring, and adopting strict prevention, control and mitigation strategies are the main options to counter COVID-19. Researchers are pacing high to design and develop effective vaccines and potent drugs / therapeutics to fight against SARS-CoV-2 / COVID-19 pandemic^{9,93}.

Public health measures are routine preventive measures, such as:

- Staying home and being isolated when sick.
- Cover the mouth and nose with flexed elbows or tissue while coughing or sneezing.
- Wash your hands often with soap and water, and apply appropriate sanitizer.
- Apply enough soap to cover your moist hands, clean all the sides of the hands, such as the backs of the hands, between the fingers and under the nails.
- If you have cough, asthma, trouble breathing, seek medical attention.
- Avoid close contact with people who are ill, even inside your family.
- Be careful that even those people with no symptoms may be able to transmit the COVID-19.
- Install Apps such as Arogya Setu app for knowing the current contact people who positive from COVID-19 disease. For self-protection, awareness and stop community transformation of COVID-19.

In severely affected countries, social distancing strategies need to be followed strictly, staying at home during lock down period; avoid mass gatherings, cancel or postpone major public events, marriages, and other social functions, closing down of schools, colleges and universities, shopping malls, government offices, libraries, museums, work places, factories and public transport systems.

Basic Concepts of avoiding SARS-CoV-2 infection in schools

Basic principles will help keep children,

teachers and staff healthy at school and help to prevent and avoid transmission and spread of this disease. Guidelines for safe practices at schools are as follows:

- Schools should ensure routine hand washing with clean soap and water, alcohol rub / hand sanitizer or chlorine solution and frequent disinfection and sanitation of school premises and surfaces.
- Sick teachers, students and other employees must not be allowed to come.
- Schools should have ample water, sanitation and waste disposal services and must follow policies for cleaning and disinfection of the school building.
- Schools can encourage social distancing and the restriction should be imposed on large gathering.
- If soap and water are not easily accessible, an alcohol-based sanitizer with at least 60% alcohol may be employed.
- Wash your hands with soap and ample of water while hands appear visibly dirty.

Promote information sharing

- Organize and follow the instructions and advisories of the national health and educational authorities.
- Share known information with staff, caregivers and students, provide up-to-date information on the disease condition, including treatment and prevention activities at schools.
- Reinforce the guardians to inform the school and health authorities if anyone at home is found infected, then ask them not to send the child to school.
- Use parent-teacher committees and other systems to encourage sharing of information. Always ensure that children's problems and issues are properly addressed, implementation of child-friendly resources, like display of posters on notice boards, in toilets, and other key locations may be helpful.

CONCLUSION

The current compilation presents an overview on the good knowledge and recent advances related to SARS-CoV-2 /COVID-19. The SARS-CoV-2 is spreading rapidly around the globe

leaving the world population in a stage of fear and huge mental trauma in the absence of any effective vaccine and therapy. Moreover, the SARS-CoV-2 is posing high global public health threats due to its highly infectious nature, rapidly increase in cases and deaths worldwide, and complex pathogenesis which is not fully understood till date. Although many drug regimens are in wide use in order to reduce the death toll and providing appropriate clinical care to the infected individuals but the search of a specific and effective therapeutic agent is needed at earliest possible time in coming future. Additionally, many companies and research institutes are on the way of vaccine development to contain this ongoing pandemic putting their best possible efforts ahead. However, prevention of the infection by social distancing and following recommended precautionary measures is the only option to stop further spread of the COVID-19 till an effective vaccine and therapy is not available. Globally, researchers, scientists, different health organizations and agencies are working days and nights with high efforts to halt further transmission and spread of this pandemic virus by following strict awareness, prevention and mitigation strategies, and improved treatment and supportive care policies. There is an urgent need of appropriate treatment for symptomatic relief to the individuals and to reduce the burden of transmission in order to minimize the infection. In addition, better understanding of COVID-19 pathogenesis, viral replication and transmission dynamics along with developing effective vaccines, drugs and therapeutics will pave the way to end this pandemic soon.

ACKNOWLEDGMENTS

All the listed author(s) are thankful to their representative universities/institutes for providing the related support to compile this work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All the listed author(s) have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

ETHICS STATEMENT

This article does not contain any studies with human participants or animals performed by any of the authors.

AVAILABILITY OF DATA

Not applicable.

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