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Review Article

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COVID 19: AN OVERVIEW OF GLOBAL OUTBREAK

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ABSTRACT

From last year, the world is threatened with the emergence and spread of a new public health crisis called novel coronavirus 2019 (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is a highly contagious disease. The virus basically originated in bats, and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province, China in late 2019. WHO has declared the ongoing outbreak of COVID-19 to be a global public health pandemic. The 2019-nCoV is transmitted by inhalation or contact with infected droplets and its incubation period ranges from 2-14 days. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. Though many peoples are asymptomatic, the disease is mild in most people in preliminary stages of its progression while in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS), and multi-organ dysfunction. The case fatality rate is estimated to range from 2-3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests, after collecting the oropharyngeal swab. Based on current published evidence, the present review systematically summarizes the epidemiology, clinical characteristics, diagnosis, treatment, and prevention of COVID-19. We hope that this review will help the public to recognize and deal with SARS-CoV-2. Besides, the authors are hopeful that the present review will also be a useful bunch for future studies by researchers, and students.

KEYWORDS: SARS-CoV-2; COVID-19; Coronavirus; Respiratory infection; Pandemic disease.

1.1 INTRODUCTION

In history, it is observed that human beings have been faced with various pandemic diseases from ancient times. And survived from such pandemic diseases, although some of them were various disastrous than each other. Now a day's world facing such conditions and fighting against a new disease called COVID-19 Coronavirus. At the outset observed in the Wuhan state of China, now quickly spreading around the world.

On 27th April of 2020 there was 3,004,334 cases of COVID-19, with 207,141 death while 882,816 recovered. It seems that the highest number of patients died in America (55,415) then Spain (23,190) and Italy (197,675). Whereas the highest number of patients (987,322) was affected in America. The highest cases of SARS-Cov-2 in the world are shown in Fig 1.[1]

As of today 26thJanuary of 2021 there are 100,300,064 cases of COVID-19, with 2,150,606 death while 72,367,490 recovered. It seems that the highest number of patients died in America (431,392) then India (153,624) and Brazil (217,712). Whereas the highest number of patients (25,861,597) are affected in America. The highest cases of SARS-Cov-2 in the world are shown in Fig 2.[1]

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[2] SARS-CoV-2, the virus that causes COVID-19 disease, is liable for the most important pandemic since the 1918 H1N1 influenza outbreak. The symptoms presently recognized by the planet Health Organization are cough, fever, tiredness, and difficulty breathing. Patient-reported smell and taste loss has been related to COVID-19 infection, yet no empirical olfactory testing on a cohort of COVID-19 patients has been performed.[3]

Corona Virus

World Health Organization officially named the disease COVID-19. International Committee on Taxonomy of Viruses (ICTV) named the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Coronavirus (COV) is a single strand RNA virus with a diameter of

80-120nm. It is divided into four types: α-coronavirus (α-COV), β-coronavirus (β-COV), δ-coronavirus (δ-COV) and γ - coronavirus (γ-COV). Six coronaviruses were previously known to cause disease in humans, SARS-CoV-2 is the seventh member of the coronavirus family that infects human beings after SARS-CoV and MERS-CoV (Middle East Respiratory Syndrome). SARS-CoV-2, like SARS-CoV and MERS-Cov, belongs to β-coronavirus.[4]

The morphology of coronavirus includes spherical or polymorphic shown in Fig. 2[Reproduced from,[6] with kind permission of the copyright holder, Elsevier, Amsterdam].The genome of the coronavirus consists of 6 and 7 open reading frames (ORFs). The ORF 1a and 1b encompass two-third of the viral genome which encodes the non-structural poly-proteins and the other four ORFs on the downstream side encode for the structural proteins such as envelope protein (E), spike protein (S), nucleocapsid protein (N), and membrane protein (M) shown in Fig 2. In some coronaviruses, the hemagglutininesterase (HE) gene is present in the region between ORF 1b and S. These structural proteins are folded and entered into the endoplasmic reticulum (ER) and transported to the Golgi transitional slot. During the replication of coronavirus, substantial amounts of structural proteins are synthesized to assemble the progeny virions.[5]

Origin

Thefirst cases were linked to the Huanan seafood market in Wuhancity of China. It has been reported that environmentalsamples obtained from the marketplace have come back positivefor the SARS-CoV-2, but the specific animal has not been identified.[7] More recently, several studies have suggested that bats could alsobe the potential natural host of SARS-CoV-2[8,9]

Transmission

The SARS-CoV-2 can be transmitted between humans via respiratory droplets. Not only the respiratory tract but also close contact, indirect contact with eye, nose, and mucous membrane also reported.[10-12] There have been no reports of fecal-oral transmission of the COVID-19 virus to date although some evidence report that the presence of SARS-CoV-2 in feces of intestinal infected patient.[13]

Incubation Period

The mean incubation period of SARS-CoV-2 is recorded to be3 to 7 days (range, 2 to 14 days) indicating a long transmission period of SARS-CoV-2.[7] Moreover, it has been reportedthat asymptomatic COVID-19 patients during their incubation periods can effectively transmit SARS-CoV-2, which is different from SARS-CoV because most SARS-CoV cases are infectedby 'superspreaders' and SARS-CoV cases cannot infect susceptiblepersons during the incubation period.[7]

Replication Cycle

Fig 3.

Clinical Symptoms

In several studies, it is found that the common clinical evidence included fever (88.7%), cough (67.8%), fatigue (38.1%), and sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), and headache (13.6%).[15] In further, a part of patients investigated with gastrointestinal symptoms, with diarrhea (3.8%) and vomiting (5.0%).[16]

Fever was defined as an axillary temperature of 37.5°C or higher. Lymphocytopenia was explained as a lymphocyte count of less than 1500 cells per cubic millimeter. Thrombocytopenia was interpreted as a platelet count of less than 150,000 per cubic millimeter. Additional expound including exposure to wildlife, acute respiratory distress syndrome (ARDS), pneumonia, acute kidney failure, acute heart failure. These results interpreted based on 291 patients who had clear information regarding the specific date of exposure.[15]

The elderly and people with implied through disorders (i.e., hypertension, chronic obstructive pulmonary disease, diabetes, cardiovascular disease), developed rapidly into acute respiratory distress syndrome, septic shock, acidosis hard to correct, and coagulation dysfunction, even resulting in the death.[17] Organ involvement confirmed by clinical features or biopsy in patients with SARS-Cov-2 is shown in Fig 4. [Reproduced from (40) with kind permission of the copyright holder, Elsevier, Amsterdam].[18]

Diagnostic Criteria

Specimen Collection

Clinical specimens for SARS-CoV-2 diagnostic testing were performed in accordance with CDC guidelines. Nasopharyngeal and oropharyngealswab specimens were collected with syntheticfiber swabs; each swab was inserted into a separate sterile tube containing 2 to 3 ml of viraltransport medium. Serum was collected in aserum separator tube and then centrifuged inaccordance with CDC guidelines. The urine andstool specimens were each collected in sterilespecimen containers. Specimens were storedbetween 2°C and 8°C until ready for testing according tothe CDC. Specimens for repeat SARS-Cov-2 testing were collected on illness days 7, 11, and 12and included nasopharyngeal and oropharyngealswabs, serum, and urine and stool samples.

Clinical specimens were tested with an RT-PCRassay that was developed from the publicly releasedvirus sequence.[19]

Detection Test

Physical Examination

Patients with mild symptoms do not show any positive signs.Patients in severe condition may face to shortness of breath, moistrales in lungs (abnormal sound),

weakened breath sounds, dullness in percussion, and increased or decreased tactile speech tremor.[20]

Computed Tomography Imaging

Computed Tomography (CT) is often found to be positive when patients with SARS-CoV-2 develop a persistent cough, fever, and unexplained fatigue. Typical CT of COVID-19 patients shown bilateral pulmonary parenchymal ground-glass opacity, pulmonary consolidation, and nodules, bilateral diffuse distribution, sometimes with a rounded morphology, and a peripheral lung distribution.[21,22]

Plasma Test

Each 80 µL plasma sample from the patients and contacts was added into 240 µL of Trizol LS (10296028; Thermo Fisher Scientific, Carlsbad, CA, USA) in the Biosafety Level 3 laboratory. Total RNA was extracted by Direct-zol RNA Miniprep kit (R2050; Zymo Research, Irvine, CA, USA) according to the manufacturer's instructions and 50µL elution was obtained for each sample. 5 µL RNA was used for real-time RT-PCR, which targeted the NP (Nucleocapsid protein) gene using AgPath-ID One-Step RT-PCR Reagent (AM1005; Thermo Fisher Scientific). The final reaction mix concentration of the primers was 500 nM and the probe was 200 nM. Real-time RT-PCR was performed using the following conditions: 50°C for 15 min and 95°C for 3 min, 50 cycles of amplification at 95°C for 10 s and 60°C for 45 s. RNAaemia was defined as a positive result for real-time RT-PCR in the plasma sample.[17]

Prevention of Infection[12]

- Handwashing with soap and water for at least 20 seconds. If soap and water are not available, use an alcohol-based hand sanitizer.
- Avoid touching eyes, nose, and mouth with unwashed hands.
- Avoid close contact with people who are sick.
- Cover a cough or sneeze with a tissue, then discard the tissue in a contained trash.
- Clean and disinfect frequently touched objects and surfaces.
- Seek medical attention if you believe you have been exposed and have symptoms.
- Adding sesame oil into the nostrils can prevent the spread of SARS-CoV-2.[23]

Treatment

No specific antiviral treatment is suggested for the SARS-CoV-2 infection. Symptomatic and supportive care is recommended together with respiratory and speak to isolation for infected individuals.

Besides this, with antibiotics and medication, the treatment mainly focused on pneumonia caused by Covid-19. Remdesivir (GS-5734) could be a 1′-cyano-substituted adenosine nucleotide analog prodrug and shows broadspectrum antiviral activity against several RNA viruses. Supported the information collected from the in vitro cell line and mouse model, remdesivir could interfere with the NSP12 polymerase even within the setting of intact ExoN proofreading activity. Remdesivir has been reported to treat the primary US case of COVID-19 successfully.[19,24]

A majority of the patients (58.0%) received intravenous antibiotic therapy, and 35.8% received oseltamivir therapy; oxygen therapy was administered in 41.3% and mechanical ventilation in 6.1%; higher percentages of patients with severe disease received these therapies.[15]

Chloroquine, an antiprotozoal, has been exhibit to be effective in vitro against the novel coronavirus SARS-CoV-2. Hydroxychloroquine, employed in autoimmune diseases like atrophic arthritis has also demonstrated in vitro antiviral activity against SARS-CoV-2 causing coronavirus diseases Covid-19. Chloroquine and hydroxychloroquine seem to inhibit the fusion of the virus to the plasma membrane by modulation of the endosomalpH. These drugs also can inhibit supermolecule replication. Chloroquine phosphate has revealed distinct efficacy in the treatment of COVID-19 with few severe adverse effects.[25] Combining chloroquine to antibiotics like doxycycline in daily prophylaxis failed to increase the chance of adverse effects.[26]

Preliminary clinical data revealed that hydroxychloroquine at 600 mg daily cured 70% of the patients at day 6 after the primary drug intake.[26] Some studies also defined that the efficacy of hydroxychloroquine was improved by combination with azithromycin.[25]

General Treatment

General treatment includes bed rest and supportive treatments, securing sufficient energy intake, maintaining a constant internal environment (water, electrolytes, and other internal environment factors) and monitoring vital signs (heart rate, pulse, blood pressure, oxygen saturation, respiratory rate).

Antiviral Therapy

Interferon α

IFNα belonging to I interferon family suppresses viral infection by directly interfering with the replication of the virus and by promoting both innate and adaptive immune responses. In vitro experiments showed that IFNα effectively inhibits the replication of SARS-CoV-2.[28,29]

Lopinavir/Ritonavir

Lopinavir/ritonavir a protease inhibitor that interferes with the replication and synthesis of human immunodeficiency virus (HIV).[29] This suggests thatlopinavir/ritonavir may exert an antiviral effect by inhibiting protein synthesis of SARS-CoV-2.[31,32]

Ribavirin

Ribavirin is a nucleoside analog with broad antiviral activity. Several studies show that it can prevent the replication of RNA and DNA viruses by suppressing the activity of inosine monophosphate dehydrogenase, which is essential for the synthesis of guanosine triphosphate (GTP). Ribavirin was widely used to treat SARS patients with or without concomitant use of steroids during the outbreak of SARS in Hong Kong.[33,34] So, ribavirin could be considered as a treatment option for COVID-19 patients.

Chloroquine

As we discussed earlier Chloroquine, a widely used antimalarial drug, has been effective in vitro against the novel coronavirus SARS-CoV-2. Various study shows chloroquine as a broad-spectrum antiviral drug.[7] Chloroquine phosphate has shown distinct efficacy in the treatment of COVID-19 with combination therapy.[25,26]

Arbidol

Arbidol is an antiviral drug widely used against influenza infection. Arbidol and arbidolmesylatewere shown to have a potent inhibitory effect in reducing the reproduction of SARS-CoV in vitro.[7]

Remedisivir

Remedisivira nucleoside analogue was observed effective against SARS-CoV and MERS-CoV in vivo.[36,37] It is also reported that, the first case of SARS-CoV2 infection in the USA was treated with intravenous remdesivir.[36]

Umifenovir

Umifenovir a derivative of indole carboxylic acidshas since been approved in Russia and China for treating prophylaxis and infections related with influenza A and B, and other arbovirus.[37] Blaising et al. reported the in vitro activity of umifenovir against SARS-CoV-1 and SARS-CoV-2.[38]

Plasma Therapy

In a certain study, it is observed that developed antibodies which are present in already cured Covid-19 patient can utilize to treat another Covid-19 patient. The convalescent antibodies present in immune plasma moderate their therapeutic effect through a variety of mechanisms. They may bind to the virus and neutralizing their infectivity or may phagocytic to virus to show therapeutic effect.[39]

This convalescent plasma treatment already used in two other coronavirus epidemics in the 21st century: SARS1 in 2003 and MERS in 2012 to the present.[40] This experimental study helps us to outbreak shows that convalescent plasma contains neutralizing antibodies.

Practice Points From an Indian Perspective

At the time of putting this on ink article, the danger of coronavirus in India is extremely low. But that will change within the next few weeks. Hence the subsequent is suggested:

- Healthcare providers should take travel history of all patients with respiratory symptoms, and any international travel within the past 2 weeks moreover as contact with sick those that have traveled internationally.
- They should set up a system of triage of patients with respiratory disease within the outpatient department and provides them an easy surgical mask to wear. They ought to use surgical masks themselves while examining such patients and practice hand hygiene frequently.
- Suspected cases should be brought up by government-designated centers for isolation and testing.
- Patients admitted with severe pneumonia and acute respiratory distress syndrome should be evaluated for travel history and placed under contact and droplet isolation. Regular decontamination of surfaces should be done. They ought to be tested for etiology using multiplex PCR panels if logistics permit and if no pathogen is identified, refer the samples for testing for SARS-CoV-2.
- All medicinal practitioners should keep themselves updated about recent developments including the global spread of the disease.
- Non-essential international travel should be avoided at this time.
- People should stop spreading myths and false information about the disease and check out to allay the panic and anxiety of the general public.[41]

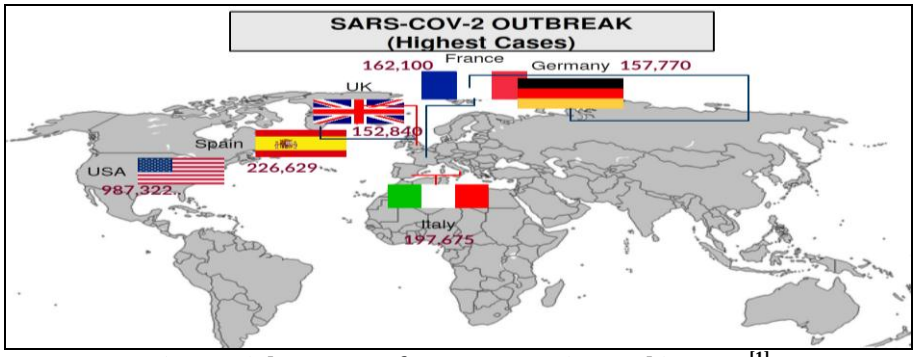

Fig. 1: Highest cases of SARS-Cov-2 in word in 2020.[1]

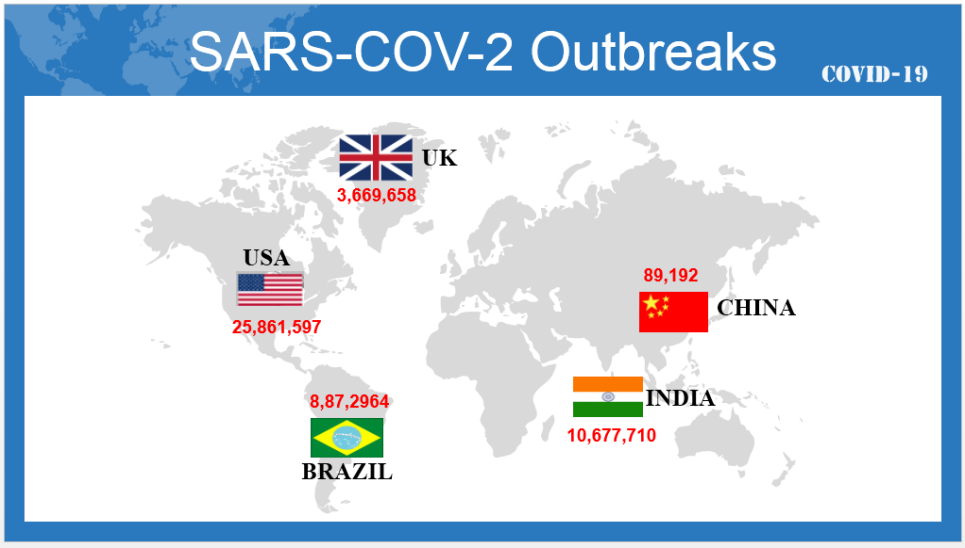

Fig. 2: Highest cases of SARS-Cov-2 in word in 2021.[1]

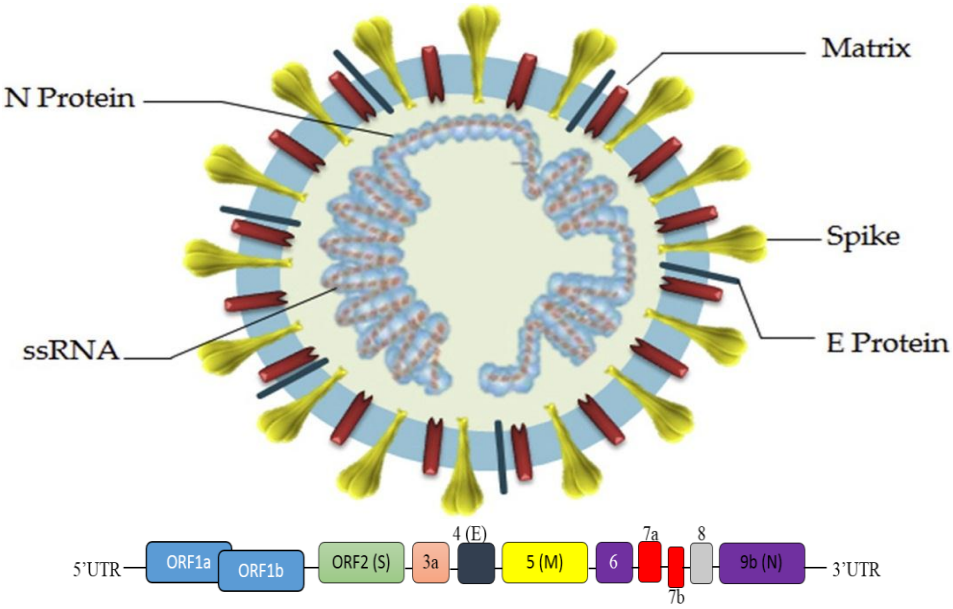

Fig. 2: Structure of corona virus and Genome sequence of corona virus.[5,6]

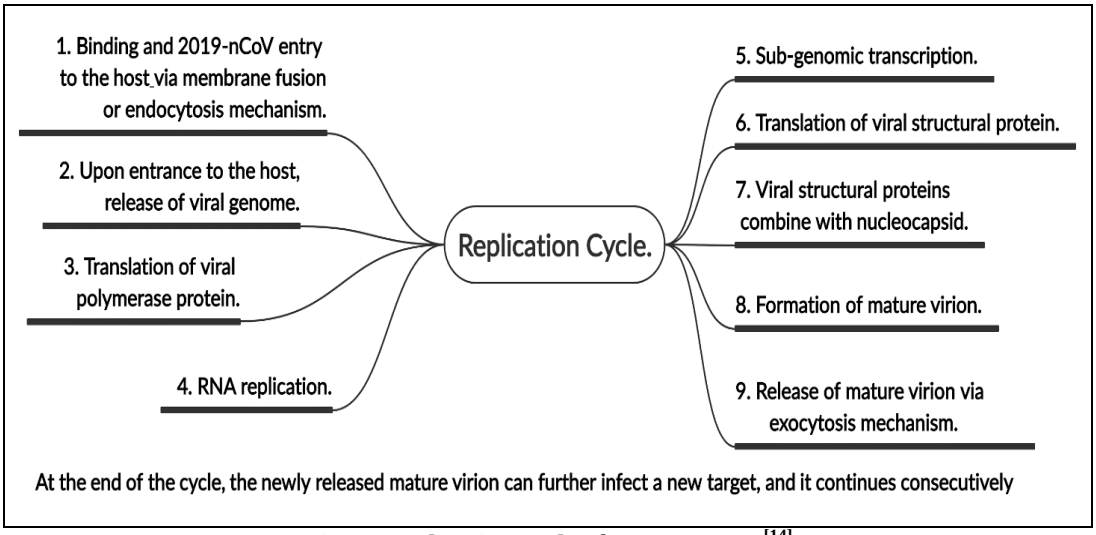

Fig. 3: Replication cycle of SARS-Cov-2.[14]

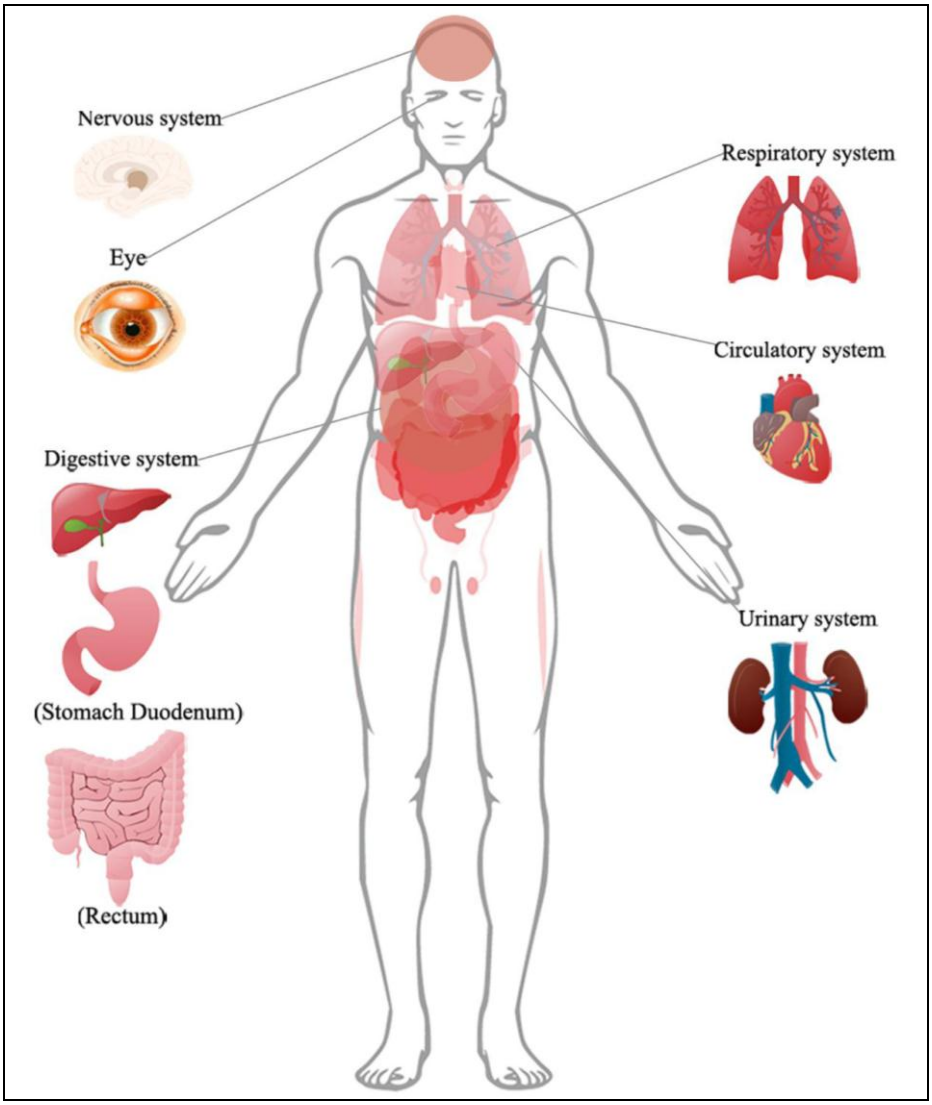

Fig. 4: Organ involvement confirmed by clinical features or biopsy in patients with COVID-19.

CONCLUSION

The outbreak of 2019-nCoV is challenging the economy, medical, and public health sectors of Chin and neighboring countries, as well. At present, it was prevalence is very low in India, but the scenario changed in few months. So, the future outbreak of the zoonotic viruses and other such pathogens is likely to continue although vaccines are available. Therefore, apart from curbing this outbreak, there is a need to take efforts to devise broad measures to prevent future outbreaks of 2019-nCoV.

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List of abbreviations

SARS-Cov-2: Severe acute respiratory syndrome Corona virus 2, H1N1: Influenza A virus subtype, MERS: Middle East respiratory syndrome, ORF: Open reading frame, CDC: The Centers for Disease Control and Prevention, RT-PCR: Reverse transcription polymerase chain reaction, and NP: Nucleocapsid protein.

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