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Kunal Batabyal
Assistant Professor and Head, Department of Veterinary, Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Samir Dey
Assistant Professor, Department of Veterinary Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Devi Prasad Isore
Assistant Professor, Department of Veterinary Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Abhiroop Banerjee
Ph.D., Department of Veterinary Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Abhishek Dharm Singh
Ph.D. Scholar, Department of Veterinary Public Health, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Tousif Mondal
M.V.Sc. Scholar, Department of Veterinary Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Soumen Samanta
M.V.Sc. Scholar, Department of Veterinary Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

Corresponding Author:
Kunal Batabyal
Assistant Professor and Head, Department of Veterinary, Microbiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata, West Bengal, India

The 2019 novel coronavirus pandemic (COVID-19): Indian scenario

Kunal Batabyal, Samir Dey, Devi Prasad Isore, Abhiroop Banerjee, Abhishek Dharm Singh, Tousif Mondal and Soumen Samanta

Abstract
COVID-19 is nowadays a highly infectious disease affecting human civilization throughout the Globe including India. A novel Coronavirus (nCoV) which was first reported from Wuhan, People's Republic of China, has now emerged as a public health emergency of international concern. The pandemic is caused by the Novel virus of the *Coronaviridae* family known as SARS-CoV-2. The outbreak was first reported in December 2019, and at present has spread in almost all over the world with more than 23 million cases causing more than 8 lakh 9 thousand deaths up to August 2020. At present India is having more than 3 million confirmed cases (3rd highest in the infection list) of novel coronavirus disease 2019 (COVID-19), with 56000+ deaths, resulting in an overall case fatality rate of 2.04 percent. By August 2020, 215 countries around the world are under the threat of the pandemic with a death rate of 5% approx. Severe acute respiratory syndrome 2 is generally transmitted via close contact with active and non-symptomatic patients and also via air droplets or aerosol routes. The virus generally infects the respiratory system and later on goes on affecting all vital organs in humans. The development of acute respiratory tract infection with fever, cough, diarrhoea, dyspnoea, headache, and breathing trouble are a few typical signs of this infection. In this background, this review will focus on virology, the nature of the infection and epidemiology, pathogenicity, symptomology, diagnostic techniques, possible remedies, and scope to overcome this threat over the mankind with special reference to the Indian perspective. This review will also focus on the key ongoing efforts to prevent the COVID-19 outbreak and identifies the needs to be incorporated in health management systems, and community response mechanisms towards improving global as well as Indian health security.

Keywords: COVID-19, control, Indian scenario, pandemic, pathogenesis, symptoms

Introduction
Coronaviruses (CoVs) belong to the family *Coronaviridae*, order *Nidovirales*, *which* is a major group of viruses mostly affecting different mammals and birds and also human beings through the zoonotic transmission. These viruses are quite active from long back causing different diseases in animals such as Transmissible gastroenteritis (in Swine) and in birds such as Avian infectious bronchitis. These were reported long back in 1931 or so. The family is such names due to their typical spherical structure decorated with large (~20 nm), club- or petal-shaped surface projections (the "peplomers" or "spikes"), which in electron micrographs of spherical particles create an image reminiscent of the solar corona. The emergence of a novel coronavirus, causing severe acute respiratory syndrome (SARS) in 2003 and another infective agent namely 'Middle East respiratory syndrome coronavirus' (MERS-CoV) in 2012 [1, 2] are having similar structure and attributes with that of the latest one - the novel coronavirus (2019-nCoV) which was reported first from Wuhan, China, in December 2019, and the disease was also named as a severe acute respiratory syndrome (SARS) by WHO. The disease condition was mentioned as novel coronavirus disease (COVID-19) and the virus is referred to as SARS-related CoV-2, or SARS-CoV-2 [3].
The emerging zoonosis caused by SARS-CoV-2 is huge and mankind is facing an ever seen pandemic that is now spread almost all over the globe. The transmission rate, death rate, risk factors associated with the susceptible groups of people, and the unpredictable nature of the infection are very much alarming points of concern in the matter of global health security [4, 5].
The COVID-19 disease had been labeled as a public health emergency of international concern by WHO in January 2020 [6, 7] and the infection rate of the epidemic is still rising [8]. The current COVID-19 pandemic in India is just similar to the worldwide pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2

[SARS-CoV-2] [9]. All the suffering countries including India are trying new health management and administrative steps towards improving the overall clinical and public health condition of general people and the responses are quite satisfactory to date.

Virology

The SARS-CoV-2 belongs to the Group 2 (β-coronavirus group) under the family *Coronaviridae*, subfamily *Coronavirinae*. Coronaviruses are a family of enveloped, positive-stranded RNA viruses (*Nidovirales* – Nido = Latin word 'nidus' – nest) having helical nucleocapsid, which mainly affects swine, dogs, cats, chickens, and humans. Virions can be pleomorphic (disc or bacilliform, 140–160 by 75–88 nm, e.g. *Bafinivirus*) or spherical, (100–180 nm d.m., e.g. *Coronavirus*) or found as a mixture of both, with bacilliform particles characteristically bent into crescents (e.g. *Torovirus*). The virus contains a single-stranded positive-sense RNA as its genome (26–32 kbp in length) and is infectious. Replication of the virus takes place in the cytoplasm of the cell. The viruses particles are typically fitted with a large, club- or petal-shaped peplomers (the "spikes") over the envelope which under electron micrographs appears like a spherical particle with radiated spikes resembling the solar corona (that's why such named - *Coronavirus*).

The SARS-CoV-2 virus is having four types of structural proteins: spike (S) protein [of two types S1 and S2], membrane (M), envelope (E), and Nucleocapsid (N) [10]. Like the SARS-CoV and MERS-CoV, SARS-CoV-2 genomic structure also contains two UTRs (untranslated regions): 5'-cap structure and 3'-poly A tail and a single ORF (open reading frame) [11]. ORF1a and ORF1b occupy the 2/3rd of the overall genome which encodes 26 NSPs (non-structural proteins) and rest 1/3rd encode accessory and structural proteins [11]. There are significant differences of ORF3b and ORF8 between SARS-CoV and SARS-CoV-2 [12]. The genome of the SARS-CoV-2 is reported to be 80% identical to the previous human coronavirus (SARS-like bat CoV). The ORF1b is the largest gene in the SARS-CoV-2 genome encoding the pp1ab protein and 15 NSPs whereas the orf1a gene encodes for pp1a protein which also contains 10 nsps [12, 13]. It (SARS-CoV-2) is closely related to the group of SARS-coronaviruses but differs from SARS-CoV slightly as it lacks 8a protein and the different number of amino acids in 8b and 3c protein in their genome [12]. The spike glycoprotein of SARS-CoV-2 is quite different having the mixed characters of bat SARS-CoV and a not known Beta-CoV [14]. Again it was confirmed that the SARS-CoV-2 also uses the same ACE2 (angiotensin-converting enzyme 2) cell receptor and mechanism for the entry to the host cell which is previously used by the SARS-CoV but the earlier one is having higher affinity [15].

There are 3 strains/types of SARS-CoV-2 viruses found in nature: Type A (very similar to those which are found in bat and pangolins. These are considered to be the root cause of the present outbreak. It is having 2 sub-clusters – one linked with the virus found in Wuhan), Type B (it is found in the outbreak of Wuhan, and is derived from the Type A virus via 2 mutations), Type C (it is the daughter of Type B developed by one mutation from B, and is spread to Europe via Singapore) [3].

The family is having 2 subfamilies, 2 genera, 23 subgenera, and approx. 40 spp. Subfamily *Orthocoronavirinae* is divided into four antigenic groups or genera depending on their genetic makeup: Group-1 (α-coronavirus, mammalian virus (e.g. Transmissible gastroenteritis virus of swine causing gastroenteritis), Group-2 (β-coronavirus, mammalian & avian virus (e.g. Bovine coronavirus causing gastroenteritis or winter dysentery), Group-3 (γ-coronavirus, avian virus (e.g. Avian Infectious bronchitis virus causing tracheobronchitis), Group-4 (δ-coronavirus, ungrouped virus (e.g. Rabbit coronavirus causing enteritis). Most of the coronaviruses cause respiratory and gastrointestinal tract infections [16]. They infect mammals, birds [17, 18]. The current SARS-CoV-2 along with SARS-CoV, MERS-CoV, has been classified into genera β-coronavirus under the *Coronaviridae* family [19].

Nature of Infection

Generally, numbers of animal coronaviruses exist in natures which have no zoonotic importance but can cause several economically significant diseases in animals of veterinary importance. Avian Infectious bronchitis (IB) is a significant economically damaging infection of poultry worldwide [20] which was first identified from North Dakota, USA, from young chickens as IBV with a worldwide distribution [21]. But this infection is not reported to be zoonotic. TGE is another highly infectious disease in the piglet caused by a Coronavirus. This virus is quite similar in structure with other Coronaviruses but quite distinct from the coronavirus Pig respiratory coronavirus (PRCV) that infects the respiratory system. TGEV causes profuse diarrhoea in pigs and piglets with almost 100% mortality in piglets [22]. Other coronaviruses can infect animals like bovine, canine, feline but not causing acute fatal diseases like these two.

But few coronavirus infections are quite zoonotic and the first human coronavirus outbreak was recorded in 1965 - HCoV-229E, this was followed by two severe outbreaks known as SARS-CoV in Guangdong, China in 2003 and MERS-CoV in recent past (2012) in Middle Eastern countries, respectively of similar capacity [2, 23, 24].

The zoonotic viruses like Severe acute respiratory syndrome coronavirus (SARS-CoV), Highly Pathogenic Avian Influenza A (H5N1), Swine Flu (H1N1) 2009, and Middle East respiratory syndrome coronavirus (MERS-CoV) are few exceptions of animal and bird viruses, causing acute lung infection and respiratory distress leading to pulmonary failure and result in a fatality in humans. Peoples of all ages can get the infection caused by SARS-CoV-2. These viruses were thought to infect only animals until the world witnessed those outbreaks as mentioned above. A severe acute respiratory syndrome (SARS) outbreak caused by SARS-CoV, 2002 [2]. Only a decade later, another pathogenic coronavirus, known as Middle East respiratory syndrome coronavirus (MERS-CoV) caused an [25].

The latest outbreak namely COVID-19 infection was first reported from the Wuhan Metropolitan in the People's Republic of China, in December 2019, and now it has rapidly spread almost all over the globe [26, 27, 28]. The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 due to its similarity with the SARS-CoV virus and the disease as COVID-19 [29, 30].

Covid-19 – Epidemiology

In December 2019, some patients were hospitalized with an initial diagnosis of pneumonia with unknown etiology that was epidemiologically linked to the seafood and wet animal market of Wuhan, Hubei Province, China [31]. The first case was in December 2019 [32], from December 19 to 29, there

were 5 patients with acute respiratory syndrome and one of them died [33, 34]. Later a total of 571 cases were found in 25 provinces in China up to January 22, 2020 [31] which increased up to 1975 cases were confirmed with 56 deaths in mainland China [35]. The outbreak spreads very quickly beyond China and 90 more cases in different countries including Taiwan, Thailand, Vietnam, Malaysia, Nepal, Sri Lanka, Cambodia, Japan, Singapore, Republic of Korea, United States, United Arab Emirates, The Philippines, India, Australia, Canada, France, Finland, and Germany were seen within next month. The first human to human transmission case was reported in the US on January 30, 2020 [36].

COVID-19 is less frequent and milder in children than adults [37]. In pregnant women, the clinical manifestations are mainly mild with few severe cases [38]. Most of the pregnant women have been reported to be asymptomatic during admission to the hospital [39]. The mean basic reproductive number from 12 model studies (the average number of secondary infections produced by a primary infection in a fully susceptible population) for COVID-19 is 3.28, with a median value of 2.79 [40]. In a study it is found that the most common viral co-infections of SARs-CoV-2 were rhinovirus/enterovirus (6.9%), respiratory syncytial virus (5.2%), seasonal coronavirus (4.3%) [41] and bacterial or fungal co-infection was 8% [42]. The health care workers are at high risk of COVID-19 due to repeated exposure to positive cases.

The rate of transmission (Ro) is the measure of transmission potential of a disease. It is the average number of secondary infections produced by a typical case of an infection in a population where it is susceptible. For SARS it is 2-4, for MERS 2.5-7, and for SARS-CoV-2 it is 2-2.5. It depends on the rate of contacts in the host population, the probability of infection transmission, and the duration of illness [43].

SARS-CoV-2 does not easily infect pet animals like dogs and cats. Very few reports are to date available indicating pet animals getting infected with this virus. Dogs and cats may show no symptoms or mild respiratory symptoms in this infection [44]. Again a few reports from New York, USA, revealed accidental SARS-CoV-2 infections in wild animals like tiger, lions, causing mild respiratory infections. The virus can cause mild gastrointestinal and respiratory symptoms in minks – a report from the Netherlands [45].

Human to human spread is the most major threat of this pandemic causing a million people to get the infection without even knowing the source. The community transmission or 3rd phase of infection is seen in many countries aggravating the spread of the virus almost all over the globe [43]. In a country like India, only a few state governments like Kerala, West Bengal, and Assam have admitted that there is positive community transmission in areas of their respective states. The report pointed out that approx. 86% of COVID-19 infections come from just a few states of the country to all 29 states, with southern India containing most of the major hotspots confirming several of cases of community transmission [46].

SARS-Cov-2 – Routes of Transmission

The transmission of SARS-CoV2 occurs via close contact with infected people; contact with contaminated surfaces (fomites) and inhalation of respiratory droplets released from infected people [40]. SARS-CoV-2 can be transmitted through direct, indirect, or close contact with an infected person through secretions of droplets (>5-10µm d.m.), aerosols (≤5µm d.m.) those are expelled out during coughing, sneezing, and talking or singing [47]. Respiratory droplets from an infected one can produce microscopic infectious aerosols by evaporation and spreading of it can occur during normal talking and breathing through these exhaled aerosols [43, 48], though the expelled particle quantity varies during the speech from person to person with an increase in time of increasing amplitude of vocalization [43]; thus a people can obtain the infection if an infective dose of virus is present in that aerosols. Some preliminary reports suggest the SARS-CoV-2 virus under experimental set up can stay viable when airborne over a short distance for a long time [49, 50].

Again, recent studies on health workers suggest no nosocomial transmission when contact and droplet precautionary measures have been adopted [51, 52]. Viable SARS-CoV-2 virus and/or RNA can be detected on surfaces (fomites) from hours to days depending on the temperature, humidity, and type of surfaces [53]; thus it is likely a mode of transmission of SARS-CoV-2 virus particularly is a great concern at health care facilities where COVID patients remain. Though there is no such published report of transmission of SARS-CoV-2 through faeces or urine some studies found viable SARS-CoV-2 from urine [54] and faeces [26, 55, 56]. The risk of blood-borne transmission is uncertain or maybe very low due to the low titre of the virus in plasma or serum [57, 58]. There is no evidence of intrauterine transmission to date. On the other hand, an infected human can be a source of infection to other mammals like dogs, cats, and farmed mink [47] and whether these infected mammals pose a potential risk to humans is unclear. The spread of a virus like SARS-Co-V can be reduced by maintaining social distancing which had been effective in controlling epidemics which lesser human-to-human transmission and thereby reducing morbidity and mortality [59]. This is quite true for COVID-19 infection too [30, 60].

The pandemic COVID-19 has four stages of transmission [61], such as Stage 1 (disease appearance through people with a travel history with everyone contained, their sources traced and no local spread from those infected); Stage 2 (local transmission when the infected individuals spread the virus to close friends or family); Stage 3 (community transmission, when infections happen in public and a source of the virus cannot be traced) and Stage 4 (when the disease becomes an epidemic in a country. Stage 1 and 2 can relatively easier to identify and control. But Stage 3 (community transmission) is quite important as random members of the community start to develop disease on large geographical scales without even knowing the source of infection. In this phase (3rd phase) of transmission, social distancing and complete lockdown of the country are the only means to check it. The recent coronavirus disease 2019 (COVID-19) outbreak was declared a "Public Health Emergency of International Concern" on 30th January 2020 by WHO [62]. The situation continues to evolve rapidly nationally and internationally leading to a pandemic now. The presence of asymptomatic patients and carriers the situation became more dangerous leading to the spread of the virus via human to human route crossing all boundaries [30].

Sars-CoV-2 – Intermediate Hosts

Bats are the natural reservoir of SARS-CoV and MERS-CoV; the RaTG13, which is a short RNA-dependent RNA polymerase (RdRp) region from a bat coronavirus having the closest identity (96.2-98.7%) in whole-genome sequence [63]. SARS-CoV (79% similarity with SARS-CoV-2) was transmitted from civet cats and MERS-CoV (50% similarity

with SARS-CoV-2) from domestic camels to humans. A recent study suggests Pangolin be the most probable intermediate host. By metagenomic sequencing, two sub-lineage of SARS-CoV-2 were found in pangolin's organ obtained from China [64]. SARS-CoV-2 was derived from the reorganization of pangolin-cCov-like virus and a bat CoV-RaTG13-like virus [98% similarity] [65]. Bats are the most probable original reservoir and Wuhan seafood may not be the only source of worldwide spreading of SaRS-CoV-2 [66]. The exact zoonotic source of SARS-CoV-2 is still to be confirmed but it is having very high genomic similarity (88-90%) with two bat-derived SARS-like coronaviruses (bat-SLCoVZC45 and bat-SL-CoVZXC21). Though it is quite a fact that SARS-CoV-2 is genetically slight distinct from that of SARS-CoV and MERS-CoV [67] but this SARS-CoV-2 (causative agent of COVID-19) belongs to the same family with these two which were first circulated in bats before transmitting via intermediate hosts to humans. SARS-CoV-2 is likely to have the almost same route of transmission to humans but can also be directly transmitted from bats to humans without an intermediate [68].

Detailed phylogenetic analysis of SARS-CoV-2 suggested that bats might act as the original reservoir of this virus but possibly there might be another unidentified intermediate host, which was likely being sold at the seafood market in Wuhan before the outbreak [31]. As the disease first emerged in the winter season (December 2019) and the bats were likely to be in hibernation, so, there should be the presence of another intermediate host, which might have played a role in spreading the infection. That's why despite about 89% genomic similarity with that of the bat-SL-CoVZC45 and bat-SL-CoVZXC21, the exact route of SARS-CoV-2 is still doubtful [14]. Again, the similarity of SARS-CoV-2 to bat SARS-CoV-like coronaviruses can be opined that bats may exist as one of the reservoir hosts whereas pangolins and snakes are thought to be the intermediate hosts [69]. The current hypothesis indicated that the consumption of different game animals (in China) may act as the missing link which is responsible for the spread of the virus from bats to human beings [70].

Studies showed that the SARS-CoV-2 virus is having specific spike protein which gets attached to the host receptor angiotensin-converting enzyme 2 (ACE2) followed by successful disease transmission in hosts. These spike proteins help the virus to enter host cells with the help of ACE2 receptors. SARS-CoV-2 virus thus can affect hosts like pigs, ferrets, cats, orangutans, monkeys, few species of bats, and humans as all have an almost similar type of ACE2 receptors against which it has affinity [68]. The current outbreak started possibly in bats and then moved to other species including human beings might be via seafood and wildlife (snakes and birds) [66, 68].

Pathogenesis of Sars-CoV-2 IN Host

The pandemic COVID-19 caused by SARS-CoV-2 is responsible for causing severe acute respiratory syndrome 2 (SARS-2) which is a systemic and respiratory disorder that can be fatal at times. In human beings after entry through the respiratory tract mainly, the SARS-CoV-2 gets attached to the ACE2 with spike protein (S). ACE2 is widely distributed in the lung epithelium, heart, ileum, kidney, and bladder [71]. Receptor ACE2 is present in monkeys and humans but not in cats, dogs, or rats. After binding with the host receptor the spike protein gets cleaved by a protease. Many proteases like TMPRSS2 (transmembrane protease serine 2), cathepsin L can cleave the coronavirus spike [72, 73, 74]. Like the proposed model of the SARS-CoV and the MERS-CoV, sequential cleavage occurs at the S1/S2 site for priming and S'2 site within the S2 subunit for activation [73]. S1 site after cleavage helps to stabilize the membrane-bound S2 and the S'2 cleavage presumably activates the spike for membrane fusion irreversibly. The virus can cause an increase in leucocyte, pro-inflammatory cytokines, C-reactive protein counts, erythrocyte sedimentation rate, and abnormal respiratory distress in COVID patients [75]. Pathogenic and zoonotic SARS-CoV-2 mainly targets the respiratory system causing severe pneumonia, ground-glass opacities in lungs, other organ malfunctions, and cardiac injury [76]. COVID-19 may show gastrointestinal symptoms indicating a role of a gut-lung axis. Pre and anti-inflammatory immune responses may be thereby signals sent by the gut microbiota. This influences the clinical symptoms of COVID-19 [77].

The main spike differences of SARS-CoV-2 with other coronavirus is the presence of furin cleavage site ('RPPA sequence') at the S1/S2 site which makes the virus very pathogenic. Once the viruses get attached to the host receptor ACE2 (attachment), they enter the host cells through endocytosis or membrane fusion (penetration). After the release of the virus in the cytoplasm, the viral RNA enters into the nucleus and the viral mRNA made new proteins (biosynthesis), then the new viral particle is assembled and released. As coronavirus blocks the ACE2 receptors the amount of angiotensin II increases in the body and leading to inflammation and pulmonary oedema. During the viral attack, there is a 'cytokine storm' with the release of several cytokines and chemokines like IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, VEGFA; and in some patients, IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα also that enhance the disease severity [78].

The severity of COVID-19 infection is associated with a huge number of active cases, increasing numbers of new cases, and case fatality rates especially in the epidemic regions of affected countries with a high population like China, India, etc. There are 3 phases of pathogenesis in the host: Phase I – infection of epithelial cells of lungs and other viscera with the release of cytokines and chemokines, Phase II – acute inflammation causing activation of immune cells, Phase III – development of severe disease after the formation of cytokine storm leading to ARDS, shock, multi-organ failure, even death of the patients [76].

The case fatality rates of this pandemic are reported to be approximately 2.84% as of Jan 25, 2020, in China and approx. 2.08% in India with the median age of the deaths was 75 (range 48–89) years [57, 79]. Human COVID patients showed higher leukocyte counts, abnormal respiratory findings, and increased levels of cytokines in the blood associated with inflammation. There may be leucopenia with leukocyte counts of 2.91 × 10^9 cells/L of which 70.0% were neutrophils. The C-reactive protein range may be noted to be 16.16 mg/L of blood, much above the normal range (0–10 mg/L). Again, ESR and bold levels of cytokines are also increased [80]. The main pathogenesis of COVID-19 infection is severe pneumonia, RNAaemia, and acute cardiac injury with significantly high blood levels of cytokines and chemokines. Few critical and severe cases may require intensive care unit (ICU) attention even as those high levels of pro-inflammatory cytokines (*viz.* IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α,

and TNFα) may aggravate disease severity [76].

Symptomology

The disease COVID-19 may create severe to mild stages of infection in human beings depending on the immune status of the hosts. The incubation period of the SARS-CoV-2 virus ranges from 5 to 14 days with an average of approx. 5.2 days [60, 81]. It was shorter among older patients (more than 70-years old) compared with those under the age of 70years. In severe and acute cases the death of the patients may occur and the average time between the appearance of first symptoms and death may vary from 6-41days with a median of 14 days [35, 57] depending on the patient's immune status [75]. COVID-19 is characterized by few common systemic disorders like fever (99% cases), dry cough (90%), fatigue (71%), myalgia (44%), sputum production (27%), anorexia (40%), body and headache (35%), haemoptysis, diarrhoea (22%), dyspnoea (31%) and lymphopenia [35, 75]; bilateral ground-glass opacities in chest CT scan [76]. The significant clinical features of COVID-19 is attacking the lower respiratory system which is evident by rhinorrhoea, sneezing, and sore throat [75, 82], infiltration of the upper lobe of the lungs which is accompanied by increased dyspnoea and hypoxaemia [83] followed by acute respiratory distress syndrome (ARDS), acute cardiac injury, and incidence of grand-glass opacities that led to death [76]. Immunocompromised and aged patients are at the highest risk of fatality in COVID-19 infection [84].

Based on severity, the typical symptoms of COVID-19 are being divided into 3 groups [29, 85] in human beings:

1) Asymptomatic to Mild Infections: Most of the infected cases (uncomplicated) are found to be either asymptomatic or very mild (approx. 81-86% of cases). The patients either show no symptoms or may show symptoms associated with very mild respiratory tract infections which are very much non-specific like fever, dry cough, malaise, headache, off fed, sore throat, muscle pain, nasal congestion, slight dyspnoea, etc. In a few cases there may be diarrhoea, haemoptysis, vomiting in mild infections [34, 35, 76]. Old aged and co-infected patients (with other diseases) may show few atypical symptoms too.

2. Acute Infections: Patients with severe to acute infections (approx. 14%) *i.e.* suffering from Acute respiratory distress syndrome (ARDS) may exhibit acute respiratory tract infections and a chest CT scan may reveal acute pneumonia, with few abnormal features such as RNAaemia, ARDS, cardiac dysfunction, and incidence of grand-glass opacities. Both the lungs may get affected showing lobar nodules, incapable of full expansion **[82]**. Respiration rate may go high up to 30/min, blood oxygen saturation level (SpO_2) may go down below 93-94%, the pulse rate may also increase in these patients. Patients may suffer from mild, moderate, and severe ARDS depending on the oxygen availability in their system. Pulmonary infiltration followed by acute respiratory distress with increasing dyspnoea with hypoxemia **[83]** and cardiac failure may happen to lead to the death of severe patients **[80]**.

3. Critical or Severe Infections: Critical and septic stage of this infection may lead to respiratory failure, sepsis, and septic shock or multiple organ dysfunction/failure or both in immunocompromised patients or patients will co-existing other diseases. In approx. 5-6% of COVID-19 patients may show these types of complications [86]. The patients show typical clinical symptoms like difficulty in breathing, fast laboured breathing, reduced urine output, tachycardia with low blood pressure, and slow pulse. Development of acidosis, high lactate level, thrombocytopenia, or hyperbilirubinemia in these patients leading to shock. This results in multiple organ dysfunction, sepsis, respiratory failure, and death [87].

Diagnosis

Around the world, COVID-19 patients are being diagnosed based on WHO interim guidance [29]. A high throughput sequencing or real-time reverse transcription-polymerase chain reaction (RT-PCR) is used to detect SARS-CoV-2 [26, 88]. It is considered as the 'Gold standard' for the detection of COVID-19 cases due to its high specificity. A Chest CT scan is also an important diagnostic approach for COVId-19 patients [89].

One of the COVID-19 case reports showed a patient at 5 days of fever presented with a cough, coarse breathing sounds of both lungs, and a body temperature of 39 °C. The patient's sputum showed positive real-time polymerase chain reaction results that confirmed COVID-19 infection [80]. As the patients infected with COVID-19 may gastrointestinal symptoms like diarrhoea, which a low percentage of MERS-CoV or SARS-CoV patients also experienced, therefore, it is important to test faecal and urine samples to exclude a potential alternative route of transmission, specifically through health care workers, patients, etc. [90].

The suspected COVID cases should have a proper history of traveling or contact with active patients or both and having no or mild symptoms like fever, respiratory illness, etc. The confirmed cases should only be categorized if there are positive reports for Real-time fluorescent RT-PCR assay detecting SARS-CoV-2 nucleic acids and the viral gene sequence is highly homologous to known new coronaviruses [76]. Serological findings increased IgM and IgG levels (at least a 4-fold increase) can detect the convalescent stage of the infection in comparison to the acute phase. Chest imaging shows several small patches on both lungs and interstitial changes more apparent in the peripheral zone of the lungs. In advanced cases, multiple ground-glass opacities, infiltration of both the lungs, consolidation of the lungs can be observed [88].

The severe COVID cases should be those who are having respiratory distress (≧30 breaths/ min), laboured breathing, lethargy, oxygen saturation ≤93% at rest, and chest imaging showing lung lesions affecting >50% of the lungs and progressing within 24-48 hours. Again the critical cases must have respiratory failure and requiring mechanical ventilation, shock, and multi-organ failure [76].

Laboratory tests like examination of blood parameters may reveal peripheral WBC count to be normal or decreased but the lymphocytic count is decreased. There may be increased blood levels of liver enzymes, lactate dehydrogenase (LDH), muscle enzymes, and myoglobin. In critically infected ones, troponin levels will become increased whereas almost all patients may show elevated C-reactive protein, ESR, and normal procalcitonin. In severe and critically ill patients elevated inflammatory factors are also seen [88].

The Novel coronavirus nucleic acid can be detected using RT-PCR and/or NGS methods from different ante-mortem samples like nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, faeces, and other specimens. The specimens obtained from the lower respiratory tract (sputum or air tract extraction) are the best for diagnosing the disease. The best diagnostic tool to detect SARS-CoV-2 is RT-PCR

which is also used in India as per the guidelines of WHO and ICMR. Different target genes like ORF1ab, RdRp, E, and N are used for screening and confirmatory diagnosis of COVID-19 using RT-PCR in many countries like China, Germany, and the USA [29].

In India, ICMR and NIV, Pune jointly developed a real-time RT-PCR assay for detecting SARS-CoV-2 targeting E, RdRp, N, and ORF genes for accurate confirmation [29]. At present, the Indian Council of Medical Research (ICMR) authorized the approx. 200+ Government and Non-government organizations to perform COVID-19 testing all over India using RT-PCR assays. The Anti-SARS-CoV-2 IgG detection ELISA ('COVID Kavach' – developed by NIV, Pune, approved by ICMR, New Delhi) is also used in India to detect IgG or IgM from patients' serum/ plasma and is also proved to be a highly sensitive and specific technique **[91]**.

For best results, the test specimens should be submitted for testing as soon as possible after collection. As the agent is in Risk Group 3 of the OIE list of pathogens, BSL-2 laboratory is mandatory for routine viral detection tests, whereas BSL-3 laboratory is recommended with all precautionary measures for all research works including culture, propagation, and neutralization examination. Triple-layer packaging of the specimen is essential with proper and fast transportation is recommended in this case [29].

Differential Diagnosis should be carried out from similar diseases caused by other known viruses such as the influenza virus, adenovirus, and respiratory syncytial virus, and *Mycoplasma pneumoniae* infections. So, integrated, modern molecular tools are to be used for fast and accurate diagnosis of SARS-CoV-2 infections [92].

Control Measures

Almost all viral infections and the COVID-19, there is very little scope for effective treatment or no scope at all. Supportive and symptomatic treatments are only practiced generally [93]. The vaccines against SARS-Cov-2 infection are under trial all over the Globe but are not available in the common market for general uses. Treatment guidelines are to be decided according to patients' conditions, results of routine blood tests result, urine analysis, detection of c-reactive protein (CRP), biochemical indicators' detection (such as a liver enzyme, myocardial enzyme, renal function, etc.), arterial blood gas analysis, chest imaging, and serum cytokines detection if necessary. Oxygen therapy should be started timely in severe and critical patients including nasal catheter and mask oxygenation and nasal high-flow oxygen therapy. Inhalation of mixed hydrogen and oxygen (H_2/O_2: 66.6%/33.3%) gases can be applied if possible. Antiviral drugs are then should be started for a better result. Critical cases should be supported by Lung protective ventilation therapy for a patient's survival. Renal replacement therapy should be accompanied by this to manage renal dysfunctions [88].

COVID-19 patients can be treated by several antiviral and other drugs which can inhibit different steps of viral replication *in vivo*. Drugs like Camostat mesylate (inhibits TMPRSS2 activity preventing viral entry in cells), Arbidol (stops S protein/ACE2 interaction inhibiting membrane fusion of the viral envelop), Chloroquine/Hydroxychloroquine (prevents endocytosis and viral entry in cells by multiple mechanisms), Lopinavir, and Darunavir (inhibits 3-chymotrypsin like protease activity, an important enzyme in viral multiplication), Ribavirin and Favipiravir (inhibits viral RNA dependent RNA polymerase stopping RNA synthesis) and Sarilumab and Tocilizumab (inhibits IL-6 activation and signaling *in vitro*). But exact efficacies of all these drugs are yet to be established [27, 94, 95].

Convalescent plasma therapy is now a very well discussed technique to overcome this crisis condition. Blood is to be collected from a recovered COVID-19 patient to collect plasma which will be the source of virus-neutralizing antibodies. This serum or plasma can be used in treating active COVID 19 patients or in susceptible hosts for prophylaxis. This therapy has few limitations like a batch to batch variability, requirement of proper blood group matching, chances of spread of several blood-borne diseases (like HIV, Viral Hepatitis, blood parasitic infections, etc.), and no definite effectiveness in long term [91, 94].

An excellent breakthrough in the treatment of COVID-19 patients had been done by stem cells with good results Abu Dhabi Stem Cell Center (ADSCC), UAE. In this effort, they collected the peripheral blood which contains few no. of free stem cells (released from the bone marrow) from the COVID-19 patients followed by separation of those stem cells. These stem cells after 'activation' are being used with liquid medicine in nebulizers which will turn the liquid medicine into the mist which when taken into by breathing will go in the lungs of the patients and cover the damaged lung cells. These stem cell mists will encourage the damaged lung cells towards auto repairing. This treatment was administered in 73 patients along with conventional treatment methods. The best thing is that all had recovered from the infection and had shown no side effects [96].

Control and prevention of the COVID-19 pandemic are quite simple *i.e.* not to be exposed to the virus. The chances of disease spread will be less if we maintain the following simple steps:

Individual-level: One should maintain social distancing and wear 3 layer masks when going out of their houses. Coming from the outside individual should take off his shoes outside and the clothes in a distant/safe place inaccessible to children. He/they should wash off their hands (frequently), mouth, and feet with soaps and water and use hand sanitizers (alcohol-based at least having 70% alcohol) for sanitizing their hands. But apply sanitizers with care as ingestion of this may be quite harmful too. Avoidance of nonessential domestic and international travel is also very necessary.

The infected people should avoid going out of their homes and maintain home quarantine with all types of precautions. He/they should follow the Doctor's advice and take medicines as directed. Critically infected people should get themselves admitted to the hospitals under Doctor's supervision for better and much wanted medical supports. Doctors and other health workers should also follow all personal protection guidelines as advised by WHO for staying safe and able to handle the outbreak without much problem.

Community-level: Total lockdown when the situation is aggravating should be implemented strictly. Lockdown can be partially lifted only when the situation is under control and the trend of new case arrival is decreasing.

Improvement of general immunity: General immunity of the common people should be increased by maintaining a disciplined lifestyle, practicing exercise and yoga, taking quality good nutritional foods [88, 94].

The development of vaccines against this pandemic is still underway. Researchers are working around the globe to find a vaccine against the SARS-CoV-2, the virus causing the COVID-19 pandemic. Till date, only one vaccine namely 'Gam-COVID-Vac' developed by the Gamaleya Research Institute in Moscow was approved by the Ministry of Health of the Russian Federation this month but the safety and efficacy of that vaccine have not yet established on a large scale Phase 3 trials [97].

Several vaccine trials are going in other countries like the USA, China, Japan, and also in India (independently and also with collaboration with other countries) but conclusive results are yet to be published. Few probable vaccine candidates which are in Phase 3 trials are as Inactivated vaccine (developed by Henan Provincial Center for Disease Control and Prevention, China), Corona Vac (developed by Sinovac Research and Development Co., Ltd., China), mRNA-1273 vaccine (developed by Kaiser Permanente Washington Health Research Institute, USA), Ad5-nCoV (developed by Tongji Hospital; Wuhan, China), etc. [97].

The Oxford University's Covid-19 vaccine candidate 'ChAdOx1 nCoV-19' ('Covishield') is also under phase 2 trials and Phase 3 trials are going on in India too in Serum Institute, Pune under the guidance of ICMR. The results are still awaited. Another Indian vaccine candidate, 'Covaxin' (developed by Bharat Biotech and National Institute of Virology, Pune, India) is in the Phase 2 trial to date. Hope within 3-4 months or so, the world will get the key to overcome this ever seeing threat to mankind – pandemic COVID-19 [97, 98].

Covid-19 - Indian Scenario

In India, the first indigenous case of COVID-19 was reported on January 30, 2020, in Thrissur district of Kerala **[99]**. On the same day, COVID-19 was declared as a "Public Health Emergency of International Concern" by the World Health Organization (WHO) [8]. The patient was a 20-year-old female, who had returned to Kerala from Wuhan University, China on 23rd January 2020 [99]. The Ministry of Health and Family Welfare (MoHFW) warned that India's testing rate needs to be increased to avoid a significant increase in the level of infection [100]. By 3rd February 2020, the cases increased to three and all were students who had returned from Wuhan, China. On 24th March 2020, the Prime minister ordered a countrywide lockdown for 21 days (25th March-14th Apri 2020, Phase I) when the confirmed coronavirus cases were approximately 500. The subsequent lockdown was carried out in Phase 2 (15th April-3rd May 2020), Phase 3 (4th May-17th May 2020), and Phase 4 (18th May-31st May 2020) [101]. During these periods, on 4th May 2020, the Government of India (GOI) divided all the districts into three zones based on the spread of the virus vis. green, red, and orange which determined the movement of activities to be permitted. Later on, 30th May 2020, it was announced that lockdown restrictions were to be lifted while further extension till 30th June 2020 was ordered for areas under containment zones. Lifting of lockdown was done in phases "Unlock" vis. Unlock 1.0 (1st June-30th June, 2020), Unlock 2.0 (1st July-31st July, 2020) and Unlock 3.0 (1st August-31st August, 2020) [102, 103, 104]. As of 15th August 2020 MoHFW has confirmed a total of 2526192 cases which includes 668220 (26.45%, active cases), 1808936 (71.61%, Discharged/ treated) and 49036 (1.94%, death) cases [105].

The disease gets transmitted by various means but the main route of transmission is via aerosol transmission. Spread via respiratory droplets and direct contact has been reported to be the primary route for its spread [40]. In early April, the WHO reported R0 (basic reproduction number) of 3.28 (1 person having the ability to infect 3.28 persons). This, however, has decreased and the latest WHO estimates it to be 1.4-2.5 (average 1.95) [43]. At present out of four stages of transmissions of COVID-19, India is in the 3rd stage *i.e.* stage of community transmissions, as per the ICMR report on 19th July 2020 and that is quite alarming too [106].

Although the disease can affect any age group, the elderly and patients with comorbidities such as cardiovascular disease, chronic respiratory disease, hypertension, and cancer are at severe risk with the prognosis being poor whereas children are at the low-risk zone [107]. In the Indian context, most severely affected people are in the age groups of 21-40 years followed by people in the age group of 41-60 years to date. Active cases are very less in children and young up to 10years of age [108]. In the case of a fatality, age groups of 30-59 and 60-75 share most no. of deaths (43% and 40% respectively) with young and babies (under 10years of age) is at the last (0.5%) [109].

The global committee is highly concerned over this pandemic and its long term consequences since it has impacted various spheres of life such as the economy, global market, agriculture, human health, industries, health care, etc. [110]. The WHO has also expressed its concern over mental health as new measures like quarantine and self-isolation have affected normal routine activities, increased loneliness, anxiety, depression, insomnia, drug use, self-harm, or suicidal behaviours [111]. The recent survey by the Indian Psychiatric Society revealed a 20% increase in mental illnesses since the coronavirus outbreak in India [112]. There is an increase in domestic violence against women and children. Millions of people have lost their jobs and many people are struggling for food as hoarding essential items and common food items had led to shortages [111].

Indian Government has taken several steps for fighting this pandemic too. Initially, the government-recognized laboratories tested samples only from those with a travel history to countries designated as high risk or those who may have come in contact with a person tested positive for the COVID-19 virus [113]. But on 20th Mar 2020, the government decided to include all pneumonia cases, regardless of travel or contact history as there was a sharp increase in the number of cases. As of 23rd August 2020, India is having more than 3millions confirmed COVID-19 cases with little more than 56000 deaths (2%) [114]. In March 2020, GOI declared COVID-19 as an epidemic (in more than a dozen states and union territories) under the provisions of the Epidemic Diseases Act, 1897 and a "notified disaster" under the Disaster Management Act, 2005, leading to the temporary closure of educational and commercial establishments. It also permits the states to spend a larger part of funds from the state disaster response fund to fight against the disease. Developments of vaccine trials have been started from April and as of current, there are 30 vaccine candidates conducting trials in various parts of India within which the Oxford University's Covid-19 vaccine 'Covishield' is expected to complete fully clinical trials very soon [98, 115]. India will surely overcome this challenge very soon.

Conclusion

The prevalence of several coronaviruses as the causative agents of a large variety of human and veterinary diseases is seen in the last few decades. The current pandemic COVID-19 caused by the novel Coronavirus (SARS-CoV-2) is having quite a similarity with SARS-CoV. The current review throws light on different aspects of the pandemic from its origin to control. To date, no vaccine is available to counter this virus, so prevention and control are only possible by maintaining WHO guidelines. This concludes with key take-home messages like the improved health system, social awareness, mass efforts, and international cooperation that are only required to combat this pandemic. Future researches should be more focused on preparing vaccines against the corona virus and other RNA viruses mainly. But now it is advised to maintain social distance only for staying safe.

Conflict of Interest

The authors of this manuscript declare that there is no conflict of interest.

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