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Review Article

Periscopic View on COVID 19 Infection: A Review

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Abstract

Recently, the world has experienced an unprecedented health risk. The unknown coronavirus (SARS-CoV-2 causing COVID-19) is causing a pandemic infection as announced by World Health Organization. It emerged from Wuhan, China in December 2019 and spread worldwide. The SARS-CoV-2 originated in bats and through yet unknown intermediary animals was transmitted to humans in Wuhan. There have been around 3,935,559 reported cases of coronavirus disease 2019 (COVID-2019) and 271,170 reported deaths to date (08/05/2020). It spreads mainly through the droplet route by inhalation or contact. Incubation period 1-14 d. Asymptomatic or patients with mild symptoms is most common of the cases; case fatality nearly 2-3%). The major symptoms are fever, dry cough, fatigue and muscle pain; less common symptoms reported are runny nose, sore throat, diarrhea, chills and hemoptysis. The SARS-CoV-2 infection is a life-threatening complication of acute respiratory distress syndrome (ARDS); in severe cases with other co-morbidities, which most commonly occurs more often in elderly or immunocompromised individuals with underlying diseases. Severe expression of the infection needs treatment in the intensive care unit with indications of acute lung inflammation, ARDS, sepsis and septic shock. Diagnosis of virus in respiratory secretions is done by special molecular tests. This review presents information about history, etiology, pathogenesis, clinical diagnostics, treatment and prevention of the infection. At present, the effective antiviral drug or vaccine is not yet available and the number of infections/death tolls surging day by day, so updated knowledge of this infection is always needed prevention for fighting the virus.

Keywords: *Coronaviruses, COVID-19, SARS-CoV-2, acute respiratory distress syndrome (ARDS), SIRS.*

Introduction

From the last months of 2019, alarming news from Wuhan, Hubei Province, China followed by spreading around China about a major outbreak of viral infections with 2019-novel coronavirus (2019-nCoV, named on 12 January, 2020 by World Health Organization, WHO)–infected pneumonia (NCIP)(Huang *et al.*, 2020; Zhu *et al.*,2020; Li *et al.*, 2020b). The infection gradually spread to other parts of the world, which was caused by a novel β-coronavirus. At present, the disease has spread to more than a dozen countries of European countries, America and Asia and Africa (Phan *et al.*, 2020a; Holshue *et al.*, 2020; Giovanetti *et al.*, 2020). Till 08/05/2020 nearly 3,935,559 reported cases of COVID-19, 271,170 deaths, and so far 1,350,951 people recovered have been reported

(https://www.worldometers.info/coronavirus). India has reported 56,561 confirmed cases of which 16,881 recovered cases till 08.05.20 (https://www.covid19india.org).

On January 30, 2020, WHO declared this outbreak a Public Health Emergency of International Concern (PHEIC) (WHO, 31 January 2020; https://www.who.int/news-room/detail/30-01-2020). It was previously known to be 2019-nCov, now referred as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by Study Group (CSG, 11 February, 2020) of the International Committee on Taxonomy of Viruses based on phylogeny, taxonomy and established practice (Gorbalenya *et al.*, 2020); the disease it caused has been named by the WHO as COVID-19 (Coronavirus Disease 2019)(WHO, 11 February 2020; https://www.who.int/dg/speeches/detail). Fortunately till date, children have been infrequently affected with no deaths (https://www.worldometers.info/coronavirus).

This article gives a periscopic view about this new virus. Since information about this virus is rapidly evolving, readers are advised to update themselves regularly. But the future itinerary of this virus is still unknown. The disease started as a 'pneumonia of unknown etiology' which was quite related to SARS outbreak in 2002-2003.Presently timely management of 2019-nCoV is the need worldwide.

Most human coronavirus infections are mild, the epidemics of the SARS-CoV in 2002-2003(Ksiazek *et al.*, 2003) and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, Saudi Arabia (de Groot *et al.*, 2013) have struck more than 10 000 swelling cases in the past two decades. The newly identified coronaviruses causing more novel and severe zoonotic events and it might only be the tip of the iceberg (Huang *et al.*, 2020).

According to WHO, about 80% of COVID-19 infection are asymptomatic or mild, 15% are severe form of infection, rest 5% are critical. The infection mortality rate (the number of reported deaths divided by the number of infection) and the crude mortality ratio (number of reported deaths divided by reported cases) will be 3-4% and 0·1% (less than seasonal influenza) respectively (WHO).

Patients from Wuhan and other provinces in China, Japan, Thailand, South Korea, USA and in other areas showed clusters of fatal pneumonia caused by 2019-nCoV with clinical presentation greatly resembling SARS-CoV. These patients might develop acute respiratory distress syndrome (ARDS), have a high probability of admission to ICU, and might die. Disease severity could be associated with the cytokine storm (Huang *et al.*, 2020).

History and evolution

Though coronaviruses were first discovered in the 1930s in domesticated chicken (Avian bronchitis virus) as an acute respiratory infection but human coronaviruses (HCoV; successfully isolation from HCoV strain B814 of patients with common cold) were discovered in the 1962 (Mahase 2020; Estola1970; Kendall *et al.*, 1962), some novel HCoVs(1960s) were described without much characterization (McIntosh *et al.*,1967; McIntosh, 1974). Subsequently all seven HCoVs (nSARS-CoV, SARS-CoV, MERS-CoV , 229E, OC43, HKU1and NL63) have a zoonotic origin from bats, birds , rodents, or other domestic animals. The most recent common ancestor of the β-coronavirus existed at 3300 BCE (Woo *et al.*, 2012). Birds and Bats are an ideal natural reservoir for the coronavirus gene pool. NL63 and 229E shared a common ancestor with a bat coronaviruses (ARCoV.2 and GhanaGrp1 Bt CoV) between 1190–1449 CE and 1686–1800 CE respectively (Pfefferle *et al.*, 2009).

The ancestors of SARS-CoV first infected leaf-nose bats (genus *Hipposideridae);* then subsequently, spread through horseshoe bats, civets, and finally to humans (Cui *et al.*, 2007). The clinical features of 229E (a prototype strain) and OC43 (in the pre-SARS era) were characterized in human volunteers (McIntosh, 1974). HKU1 (in 2005) and NL63 (in 2004) were first isolated from a pneumonia patient and a child with bronchiolitis respectively (van der Hoek *et al.*, 2004; Lau *et al.*, 2006; Zhu *et al.*, 2020). HKU1 and NL63 reported to cause mild respiratory diseases around the world (van der Hoek *et al.*, 2005). 229E OC43, HKU1 and NL63 are community

acquired HCoVs causing severe lower respiratory tract disease only in rare cases in human host also (Wang *et al.*, 2020c).

SARS-CoV does not cause mild infections like its ancestors. SARS-CoV infection turned into a SARS epidemic in 37 countries (case fatality of 9.6%) (Perlman and Netland,2009). In the past two decades, two severe disease events (mortality rate 11-34%) have been recorded by transmission of animal β-coronaviruses to humans. In 2002–2003, the first such instance occurred in Guangdong province of China when a new β-coronavirus crossed from bat to humans through palm civet cats, affecting 8422 people mostly in China and Hong Kong and caused 916 deaths before being contained (Chan-Yeung and Xu, 2003). In 2012, a decade later, in Saudi Arabia, the MERS-CoV, with bat origin, emerged with intermediate host dromedary camels by affecting 2494 people and 858 deaths. Exported MERS cases with sporadic recurring outbreaks were also reported outside Arabian world since 2012 with186 confirmed cases in 2015 in South Korea. Clinical symptoms ranges from asymptomatic to critical ARDS also (Zumla *et al.*, 2015; Zhou *et al.*. 2017; Yeung *et al.*, 2016; https://www.who.int/emergencies/mers-cov/en/).

Through evolution, the reservoir hosts of these viruses are selected. During the long period of this selection and mutual adaptation, they usually cause very mild (by 229E, HKU1, NL63 and OC43) or non-pathogenic diseases, remain dormant in their native reservoir hosts. However, when this animal virus enters a new host like humans, a new round of adaptation starts with more severe form of the disease (Fung *et al.*, 2020) like the SARS-CoV (Zhong *et al.*, 2003; Drosten, *et al.*, 2003) and the MERS-CoV outbreak (Zaki *et al.*, 2012). These viruses' remains in the circulation in camels and in December 2019 the SARS-CoV-2 coronaviruses emerged in Wuhan of China and presently spreading worldwide (Zhu *et al.*, 2019).

Epidemiology

The transmission and source(s) of SARS-CoV-2 were elucidating. In SARS-CoV-2 infection, human-to-human transmission occurs mainly within family members, friends and relatives who intimately contacted the infected patients or incubation carriers. People recently travelled to Wuhan or non-residents people who contacted patients from Wuhan got infected (Guan *et al.*, 2020). National Health Commission of China on 14 February 2020 reported that 3.8% of COVID-19 patients were transmission between healthcare workers. Consumption of wild animals or direct contact with intermediate host animals was suspected to be the primary route of SARS-CoV-2 transmission (Guo *et al.*, 2020).

Since 12 December 2019, from Wuhan seafood market, the first epidemic of unknown acute respiratory tract infection broke out. Bat may be the potential reservoir of SARS-CoV-2 (Giovanetti *et al.*, 2020; Paraskevis *et al.*, 2020)as known also bats are the natural reservoir of SARS-CoV-like, MERS-CoV-like viruses, and a wide variety of CoVs (Hampton, 2005; Banerjee *et al.*, 2019; Li *et al.*, 2005). Upon virus genome sequencing, the SARS-CoV-2 showed 96.2% overall genome sequence identity to bat CoV RaTG13 (Zhou *et al.*, 2020) and 79.5% identity to SARS-CoV (Zhou *et al.*, 2020); thus bat CoV and human SARS-CoV-2 might carve up the same ancestor, although bats were not sold in Wuhan seafood market (Wu *et al.*, 2020). Protein sequences alignment and phylogenetic analysis (Liu *et al.*, 2020) revealed similar residues of receptor in various species (Bat, swine, civet), which elucidate possibility of alternative intermediate hosts, like turtles, pangolin and snacks.

Coronavirus family, morphology and structure

Coronavirus is an enveloped virus (60 nm to 140 nm in diameter) with a RNA polycistronic genome, single stranded positive-sense strand (length 26 to 32 kb) referred for its solar corona (Latin word *corona* means crown; transmission electron microscopy imaging) like appearance with 9-12 nm-long surface spikes (Wang *et al.*, 2020a). It belongs to the family Coronaviridae and the order Nidovirales (subgenus *Sarbecovirus*, subfamily *Orthocoronavirinae*) (Huang *et al.*, 2020; Richman *et al.*, 2016, Zhu *et al.*, 2020). The severe form of this family of HCoVs includes

the recent nCoV/β-coronavirus (COVID-19), SARS-CoV and MERS-CoV with the less severe ones like HKU1, NL63, OC-43 and 229E *(*229E and NL63 belong to α-coronavirus) (Zhou *et al.*, 2020). The α- and β-CoV are able to infect mammals, but γ- and δ-CoV infect birds (Guo *et al.*, 2020).

There are four major structural proteins [small envelope (E) protein, matrix (M) protein, spike (S) like surface glycoprotein, and nucleocapsid (N) protein] on the envelope encoded by the coronaviral genome. Several other accessory proteins also interfere with the host innate immune response (Cui J *et al.*, 2019). The spike protein on the envelope binds with angiotensin-converting enzyme 2 (ACE2) receptor for fusion with host cell membranes and to enter respiratory mucosa into the host cell (Hampton,2005) (through S1 and S2 distinct functional domain of spike protein) (Kirchdoerfer *et al.*, 2016; Xu *et al.*, 2020; Velavan and Meyer, 2020; Phan *et al.*, 2020a,b).

Genomic characteristics

The genome deep sequencing of SARS-CoV-2 was done by clinical samples from several laboratories (Zhy *et al.* , 2020; Zhou, *et al.*. 2020 ; Lu *et al.*, 2020b; Chen *et al.*, 2020c; Chen *et al.*, 2020b; Chan *et al.*, 2020). The SARS-CoV-2 viral genome is around 29.8 kilobase, with a G+C content of 38%. It has six major open reading frames (ORFs) in total common to coronaviruses and some other accessory genes (Zhou *et al.*, 2020; Chan *et al.*, 2020). The genome sequences of viruses from different patients are highly conserved (Zhou *et al.*, 2020; Lu *et al.*, 2020b; Xu *et al.*, 2020), revealing that this human virus evolves recently.

In groundwork report, complete viral genome analysis discloses that the virus shares 88% sequence homology to two bat-derived SARS-like-coronaviruses (Lu *et al.*, 2020b). Besides, phylogenetic analysis and protein sequences alignment (Liu *et al.*, 2020) revealed that analogous residues of receptor were seen in many species, which presented more possibility of intermediate alternative hosts, like pangolin, turtles, and snacks (Guo *et al.*, 2020). SARS-CoV-2 uses ACE2 receptor like the SARS-CoV (Zhou *et al.*, 2020), to infect humans.

The 2019-nCoV mutate faster than DNA viruses (Tang *et al.*, 2020). 2019-nCoV has the inherent attribute of high mutation rate, as an RNA virus. Due to high mutations and recombination rate of this virus, diverse viral strains are evolving with new features. But the presence of genome encoded exonuclease, lower the mutation rate in comparison to other RNA viruses (Zhou *et al.*, 2020; Tang *et al.*, 2020; Sanjuán and Domingo-Calap,2016).

Deep meta-transcriptomic sequencing on Wuhan-Hu-1 coronavirus (WHCV), recently showed 16 predicted non-structural proteins (NSP). WHCV and SARS-CoV exhibits similarity to S-glycoprotein gene and receptor-binding domain (RBD), reported by some phylogenetic and genomic analysis, indicating their capability of direct human transmission. No amino acid substitutions occurred in NSP7, NSP13, envelope, matrix, or accessory proteins (p6 and 8b) at the protein level between WHCV and SARS-CoV , except in NSP2, NSP3, spike protein, underpinning the RBD (Wu *et al.*, 2020). Mutation in NSP2 and NSP3 play a role in differentiation mechanism and infectious capability of SARS-CoV-2(Angeletti *et al.*, 2020). Thus transmission and host tropism between SARS-CoV-2 and SARS-CoV need to be explored for future therapeutic targets (Zhang *et al.*, 2020a). Report showed that SARS-CoV-2 had been mutated in various patients in China as analyzed from the genotypes of COVID-19. Moreover, the degree of diversification of SARS-CoV-2 is smaller than the mutation of H7N9 avian influenza (Wu *et al.*, 2015). L type (~70%) and S type (~30%) are the two prevalent evolvement types of SARS-CoV-2, as revealed by population genetic analyses of 103 SARS-CoV-2 genomes. The L type strains is evolutionarily more aggressive and contagious posing concern for virologists to closely monitor the virulence and epidemic of 2019-nCoV (Tang *et al.*, 2020).

Transmission and clinical characteristics

As an emerging acute respiratory infectious disease, COVID-19 spreads primarily by droplets, direct contact and respiratory secretions (Li *et al.*, 2020b) through the

respiratory tract, in a low infective dose (Lee and Hsueh, 2020); fecal swabs and blood in severe cases (Zhang *et al.*, 2020a,b); largely transmitted from symptomatic patients through inhaled or by touching contaminated surface infectious droplets (and fomites) generated during sneezing and coughing. Acquired Infection is then spread by touching the eyes, nose and mouth. The virus is also present in the stool and contamination water supply and consequent aerosol transmission through feco-oral route (Zhu *et al.*, 2020). These infected droplets can deposit on surfaces with a spread of 1–2 m for days in favorable atmospheric conditions. All ages are at risk. It can also transmit from asymptomatic people and before the onset of symptoms (Giovanetti, 2020).

The virion entry interaction between S protein and human ACE2 receptor (hACE2) on lung alveolar epithelial cells may help to understand the viral infection routes and disease manifestations. The present SARS-CoV-2 has the incubation period is 1–14 d and is contagious during the latency period (Jin *et al.*, 2020). It is vastly transmissible in humans, especially in the elderly (> 65 years) and immunocompromised people.

No difference in viral burden between asymptomatic and symptomatic people was noted. Studies showed higher viral loads in the nasal cavity than in the throat (Banerjee *et al.*,2019). Patients remain infectious as long as the symptoms persist or may extend on clinical recovery also. The virus can be killed in less than a minute by common disinfectants like hydrogen peroxide, sodium hypochlorite, etc. (Li, 2005). As per current information, transplacental transmission from pregnant women to their fetus has not been described (Chen *et al.*, 2020d; Aiping *et al.*, 2020). ACE2, a carboxypeptidase, essentially removes carboxy-terminal of basic or hydrophobic amino acids. ACE2 is normally expressed in human lungs on type-I and type-II lower alveolar epithelial cells.ACE2 more expressed in mouth than tongue. The high affinity of SARS-CoV-2 for cellular receptor present in the upper respiratory tract causes faster transmission (Banerjee *et al.*, 2020).

The current data on the COVID-19 showed that it might be initially hosted by bats (*Hipposideros larvatus*) (Gouilh *et al.*, 2011), and then transmitted to humans through pangolin (Lam *et al.*, 2020) or various wild animals (Lu *et al.*, 2020a; Zhang *et al.*, 2020a,b) sold at the Hunan market but then subsequently it took human-to-human transmission route with mild common cold-like symptoms, but in immunecompromised patients severe lower respiratory tract infection develops (Pene *et al.*, 2000). The virus can co-infect different vertebrates species including humans and affect gastrointestinal, respiratory and CNS infection; with life-threatening ARDS in some critically ill patients (Leung *et al.*, 2003; Xu *et al.*, 2005; Lu *et al.*,2020a).

The superspreading events in the SARS-CoV transmission in 2002 are thought to be the release of large amounts of virions. The use of immunosuppressive agents and mutation of virus susceptibility genes encoding restriction factors in host antiviral defense might boost viral replication with shedding of large amounts of virus (Stein, 2011). Thus host antiviral immune response facilitates superspreading. SARS-CoV was identified and isolated as the causative agent of SARS (Peiris *et al.*, 2003) with lower respiratory tract infection, cytokine storm and poor outcome in patients.

Virus replication, infection and pathogenesis

Cellular entry receptor for SARS-CoV-2 (like SARS-CoV), is the ACE2 found in the humans lower respiratory tract (Zhou *et al.*, 2020; Jia *et al.*, 2005). ACE2 protein is abundantly present on lung alveolar epithelial cells and in enterocytes of small intestine (Hamming *et al.*, 2004). ACE2 regulates both human-to-human and the cross-species transmission (Wan *et al.*, 2020). S-glycoprotein on the surface of coronavirus can attach to the ACE2 on the surface of human cells (Tortorici and Veesler, 2019). Virus-receptor binding affinity is a critical step in SARs-CoV infection. S-glycoprotein includes two subunits, S1 and S2 (Zhang, *et al.*, 2014). S1 determines the cellular tropism and virus-host range through its RBD. S2 causes virus-cell membrane fusion by heptad repeats 1 (HR1) and HR2,

the two tandem domains (Xia *et al.*, 2020;Yu *et al.*, 2020). The viral genome RNA, after the membrane fusion, is released into the cytoplasm. The uncoated RNA translates two polyproteins, pp1a and pp1ab (de Wilde *et al.*, 2018). The pp1a and pp1ab encode non-structural proteins and form the replication-transcription complex (RTC) in double-membrane vesicle (Sawicki and Sawicki, 2005). RTC continuously replicate to form a nested set of subgenomic RNAs (Hussain *et al.*, 2005) to encode structural and accessory proteins. The newly formed genomic RNA, envelope glycoproteins and nucleocapsid proteins assemble to form viral particle buds (Perrier *et al.*, 2019). Lastly, the viruses are released through fusion of virion-containing vesicles with the plasma membrane. Human cells expressing ACE2, but not human APN (Aminopeptidase N) or Dipeptidyl peptidase-4 (DPP4), were more viable for SARS-CoV-2 entry using the ACE2 receptor (Letko *et al.*, 2020). The pathogenesis is controlled by the balancing reaction between the virus and host antiviral defense. The virus and host co-exist peacefully through years of co-evolution in mutual benefit in a balancing environment. The viral pathogenesis of SARS-CoV-2 is revealing each day, but idea of host antiviral immunity can be elucidated from other human pathogenic virus families (Fung *et al.*, 2020).

Symptoms, complications and clinical presentation

Common symptoms at onset of illness were fever, dry cough, sore throat, shortness of breath (dyspnoea), and fatigue or myalgia, lymphopenia; less common symptoms were headache, sputum production, haemoptysis and diarrhea, vomiting. However, gastrointestinal and upper respiratory symptoms were rare. Thus the viral tropism of SARS-CoV-2 is different from SARS-CoV (Lee *et al.*, 2003), influenza (Wang *et al.*, 2016) and with MERS-CoV (Assiri *et al.*, 2013).

All patients had pneumonia with abnormal findings on chest CT imaging (Huang *et al.*, 2020) reflecting that the chest was ground-glass opacity and bilateral patchy shadowing(Guan *et al.*, 2020). Sometimes a rounded morphology with a peripheral lung distribution was analyzed from patients (Chung *et al.*, 2020). However, a part of confirmed patients showed normal CT images. The diagnostic sensitivity lies in virus RNA detections and evaluation of clinical symptoms.

This disease was caused by virus-stimulated pneumonia demonstrated by clinicians according to clinical signs and symptoms like increased body temperature, lymphocytopenia and leucopenia (or WBC in normal range), new pulmonary infiltrates visible on chest radiography and no apparent improvement after antibiotics treatment for three days. Most of the early cases appeared by contact history with the Wuhan seafood market; thereafter, the disease transmitted by human-to-human contact (Zhou *et al.*, 2020).

The most vulnerable cluster in corona pandemic is elderly, hypertensive, immune compromised (diabetes, cardiovascular disease, chronic obstructive pulmonary disease) individuals who may rapidly develop septic shock, ARDS, metabolic acidosis and coagulation dysfunction, multiple organ failure, even leading to the death (Huang *et al.*, 2020).

The malnourished, cancer patients as well as pregnant women were also susceptible. Predictable pattern of clinical course is somehow utilizable. Flu-like symptom like fever, dry cough, headache, fatigue and myalgia (with back pain), nausea, abdominal discomfort, loss of smell, anorexia with little diarrhea persist on around day 5. Worsening symptoms at this period includes shortness of breath due to bilateral viral pneumonia causing damage to lung parenchyma (as observed by transverse chest computerized-tomography images) and even death. On day 10, cytokine storm triggers, consequently with ARDS and multi- organ failure. In moderate to severe cases patients' usually hypoxic stage present without dyspnea (Zhou *et al.*, 2020).

China reported 15% cardiac cases with serious final outcome. In major of the reported chest X-rays, ground glass opacities or bilateral interstitial pneumonia are seen, but chest auscultations are of no help. Chest X-ray findings does not correlate well mostly with the hypoxia. Reported blood tests showed, in most cases, low WBC count ,low platelet count, elevated CRP, CPK, LDH, D-dimer, ALK -

phos/AST-ALT and ferritin levels whereas procalcitonin concentration in normal range. If the ratio of absolute neutrophil count to absolute lymphocyte count is greater than 3.5, then it may predict poor outcome. Cytokine storm is reflected by high level of IL-6, IL-10, IL2, IL7, GSCF, IP10, MCP1, MIP1A, and TNFα (Mehta *et al.*,2020; Huang *et al.*, 2020). Complications related to disease severity includes ARDS, arrhythmia, RNAaemia, shock, acute kidney injury, liver dysfunction acute cardiac injury and secondary infection (Huang *et al.*, 2020; Wang *et al.* 2020a). The aged male with ARDS and comorbidities showed a higher death risk due to their weak immune system (Wang *et al.* 2020a)

Diagnosis, precaution, prevention

The viral research institution in China has conducted the preliminary identification of the SARS-CoV-2 by observing its morphology in electron microscopy using the classical Koch's postulates (Lu *et al.*,2020a). The clinical diagnosis method of COVID-19 disease is by nucleic acid detection in the throat swab and nasal / other respiratory tract sampling (s) or by real-time PCR and further confirmed by next-generation sequencing [Guo *et al.*, 2020]. Initial plasma concentration of IL1B, IL1RA, IL7, IL8, IL9, IL10, GCSF, basic FGF, GMCSF, IFNγ, IP10, MCP1, MIP1A, MIP1B, TNFα, PDGF, and VEGF were higher in both ICU and non-ICU patients than healthy subjects. Plasma levels of IL5, IL12p70, IL15, RANTES and Eotaxin, were comparable with healthy adults (Huang *et al.*, 2020).

Disease onset may show speedy advancement to organ dysfunction (such as shock, acute cardiac injury, etc) and in severe cases even death (Wang *et al.*, 2020a; Chen *et al.*, 2020c). Patients during the period might show normal or lower WBC counts (leucopenia; less than 4×10^9/L), thrombocytopenia or lymphopenia (lymphocyte count $<1{\cdot}0 \times 10^9$/L), increased prothrombin time, increased C-reactive protein level with extended activated thromboplastin time. Procalcitonin within normal range of patients on admission (<0·1 ng/mL) (Huang *et al.*, 2020). Procalcitonin may only increase in case of bacterial coinfection.

Initial investigations included a complete hemogram, coagulation contour, and serum biochemical investigation (like liver and renal function, lactate dehydrogenase, creatine kinase, and electrolytes). Nasal and pharyngeal swabs, sputum, bronchoalveolar lavage fluid, or bronchial aspirates were tested for common viruses, like adenovirus, influenza, avian influenza, parainfluenza virus, respiratory syncytial virus, MERS-CoV and SARS-CoV. Routine bacterial and fungal investigations were also performed.

Treatment

There are no specific medicines or vaccines for COVID-19 at present. Clinical experiences and few clinical trials in affected pandemic areas form the descriptive reports of treatment procedures. The viral genome sequencing of SARS-CoV-2 facilitates epidemiologic tracing, rapid diagnostic evaluation, and management of therapeutic and preventive strategies. Inavailability of effective antiviral therapy, current treatments against COVID-19 mainly highlighted on respiratory and symptomatic support according to the Diagnosis and treatment Protocol(http://www.gov.cn/zhengce/zhengceku/2020). Though all patients received oxygen therapy by WHO recommendations, patients with refractory hypoxemia received extracorporeal membrane oxygenation (ECMO) (WHO, https://www.who.int/publicationsdetail). In some critical cases, immunoglobulin G and convalescent plasma as rescue treatment were given (Chen *et al.*, 2020a). Neuraminidase inhibitors (like oseltamivir, peramivir etc) used for influenza virus, were not recommended for COVID-19(Wang *et al.*, 2020a, b; Li *et al.*, 2020a).

There are no clinical trial data supporting any prophylactic therapy. Though above 300 active clinical trials are ongoing, no randomized clinical trials (RCTs) with outcome of potential therapy in suspected or confirmed COVID-19 patients is noted (Sanders *et al.*, 2020). Chloroquine blocks SARS-CoV-2 *in vitro* at a half-maximal effective concentration (EC_{50}) whereas hydroxychloroquine has a lower EC_{50} *in vitro* (Yao *et al.*, 2020). Ongoing Clinical trials of remdesivir (formally known as GS-

5734) to evaluate the antiviral activity and safety in patients with mild/ moderate/ severe COVID-19 (NCT04292899, NCT04292730, NCT04257656, NCT04252664, NCT04280705) (Sanders *et al.*, 2020) but it is not currently FDA-approved. Till date, favipiravir and corticosteroids (should not be used unless otherwise indicated) has not been reported or may be used in limited regime for COVID-19. Tocilizumab (FDA-approved), a monoclonal antibody IL-6 receptor antagonist, with RCTs alone or in combination in COVID-19 patients are underway in China (NCT04310228, ChiCTR200002976) (https://www.china law translate.com/wp-content/uploads/2020/03/Who-translation.pdf). Hyperimmune immunoglobulins or convalescent plasma is another potential adjunctive therapy for COVID-19 (Chen *et al.*, 2020a). The WHO clinical management guidance (as of March 13, 2020) recommended no specific anti-COVID-19 treatment for patients for confirmed COVID-19 patients (WHO March 13), early recognition, treatment of secondary bacterial infections or sepsis and emphasized on supportive care depending on severity of disease or evidence-based ventilator supervision for ARDS (Sanders *et al.*, 2020).

Conclusion

Two epicenters of the pandemic novel coronavirus Covid-19 created were at first the Hubei Province in People's Republic of China and currently in Europe. SARS-CoV-2 is more infective and pathogenic than its other family members like SARS-CoV and MERS-CoV. The alarming wide spread of the disease in different countries, the increasing number of reported cases raises a grave concerns about the future projectile of infection of this virus. It is of utmost importance to understand the pathogenesis, molecular mechanism of transmission, replication and viral entry and future treatment directive of this viral strain.

The outbreak of COVID-19 spread across China fast and has outbreak to 227 countries outside of China as of 8 May 2020 (COVID-19 dashboard, CSSE, 08.05.20). Scientists have characterized the novel coronavirus and made progress for future therapies and vaccines for the virus. We have abridged the current knowledge of SARS-CoV-2. The ongoing supporting treatments and potent antiviral drugs, includes lopinavir/ritonavir, chloroquine, or and remdesivir and others should be supported with definite clinical trials. the provides the basis of potential research for developing targeted treatments. The evolutionary ancestries from the original host, the cross-species or human-human transmission need to be projected.

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Conflicts of Interest

The authors declare that the research review was conducted in the absence of any commercial or economic associations that could be construed as a potential conflict of interest.

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