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A REVIEW ON RECENT ADVANCES IN COVID-19 MANAGEMENT

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ABSTRACT

The world has experienced several epidemics posing serious threat to global public health, including the 2002 severe acute respiratory syndrome (SARS) epidemic that caused 800 deaths out of about 8,000 cases, the 2009 H1N1 pandemic with 18,500 deaths, the 2012 Middle East respiratory syndrome (MERS) epidemic that caused 800 deaths out of 2,500 cases, the 2014 Ebola outbreak with 28,616 cases and 11,310 deaths, and the current coronavirus disease (COVID-19) pandemic with more than 1,565,292 deaths out of over 68,659,920 confirmed cases till now. and is affecting 213 countries all over the world. Coronavirus (CoV) disease-2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome- CoV-2. The disease started in 2019 in Wuhan, China, and has spread globally, resulting in a pandemic. Common symptoms include fever, cough, and shortness of breath. Muscle pain, sputum production, and sore throat are less common symptoms. While the majority of cases result in mild symptoms, some progress to pneumonia and multiorgan failure. The deaths per number of diagnosed cases is estimated between 1% and 5%, on an average but varies by age and other health conditions. The infection is spread from one person to other via respiratory droplets, often produced during coughing and sneezing. It takes 2–14 days to develop symptoms from the day of exposure. Reverse transcription- polymerase chain reaction from a nasopharyngeal swab or oropharyngeal swab is the standard method of diagnosis. The infection can also be diagnosed from a combination of symptoms, risk factors, and a computerized tomographic scan of the chest showing features of viral pneumonia. Measures recommended to prevent the disease include frequent hand washing, maintaining safe distance from other people, and not touching one's mouth eyes and nose. The use of masks is recommended for those who are suspected to have the virus and to their caregivers, besides the general public. As of now, there are currently more than 50 COVID-19 vaccine candidates in trials. WHO is working in

collaboration with scientists, business, and global health organizations through the ACT Accelerator to speed up the pandemic response. Management of COVID-19 involves treatment of symptoms, supportive care, and experimental measures. In this review all relevant information about Corona virus management is given.

KEYWORDS: Coronavirus; COVID-19; SARS-CoV-2; Infectious disease; Possible management.

INTRODUCTION

Coronaviruses (CoVs) are enveloped, single- stranded RNA viruses ranging from 60 to 140 nm in diameter with spike- like projections on its surface, giving it a crown- like appearance under the electron microscope, hence the name CoV. Four CoVs namely HKU1, NL63, 229E, and OC43 have been in circulation in humans, and generally cause mild respiratory disease.[1] On December 31, 2019, a cluster of cases of "pneumonia of unknown origin" in people associated with the Wuhan's Huanan Seafood Wholesale Market has been reported in Hubei province, China. Only a few days later, Chinese health authorities confirmed that this cluster was associated with a novel CoV and was named CoV disease-19 (COVID-19) by the World Health Organization (WHO).[2] COVID-19 is closely associated with bat- derived severe acute respiratory syndrome (SARS-CoV)- like CoV (bat-SL-covzc45 and bat-SL-covzxc21) (with 88% identity), but is far away from SARS-CoV (about 79%) and MERS-CoV (about 50%), by 8th December 2020 number of reported cases are 68,659,920 worldwide with 1,565,292 deaths reported. India has reported around 9,735,975 cases with 1,41,398 mortality till 8th December 2020.[3]

Aetiology and origin of SARS-CoV-2

Coronaviruses (CoVs) are positively sensed single-stranded RNA viruses that belong to the order Nidovirales, family Coronaviridae, subfamily Orthocoronavirinae with 4 genera: alpha, beta, delta, and gamma coronaviruses.[4] Alpha CoVs and beta CoVs originated from bats and rodents while delta CoVs and gamma CoVs have their origins from avian species.[5] The beta CoVs including SARS- CoV-1 was isolated from bats in 1992 with civet cats being the intermediary host; MERS-CoV was isolated from dometry camels in 2003; and of course, the currently circulating SARS-CoV-2 formally referred to as 2019 novel coronavirus (2019-nCoV) causing COVID-19. SARS-CoV-2 has a pleomorphic and circular structure with a diameter of about 60-140 nm. It can be transmitted from human-to-human by respiratory

droplets from sneezing, coughing, and aerosols, with symptomatic people being the major source of transmission. It has a dynamic incubation period of about 2 to 14 days.[6]

Epidemiology of Coronavirus Disease-19

A cluster of pneumonia cases of unknown origin in Hubei province, China, caused concern among health officials in late December 2019. On December 31, an alert was issued by the Wuhan Municipal Health Commission. A rapid response team was sent to Wuhan by the Chinese Center for Disease Control and Prevention (China CDC), and a notification was made to the WHO. Likely potential causes including influenza, avian influenza, adenovirus, SARS-CoV, and MERS-CoV were ruled out. Epidemiological investigation implicated Wuhan's Huanan Seafood Wholesale Market, which was shut down and disinfected, and active case finding was initiated and vigorously pursued. On January 7, 2020, the causative pathogen was identified as a novel CoV, and genomic characterization and test method development ensued. Now named 2019-nCoV, the virus is distinct from both SARS-CoV and MERS-CoV, yet closely related. Early cases suggested that COVID-19 (i.e., the new name for disease caused by the novel CoV) may be less severe than SARS and MERS. However, illness onset among rapidly increasing numbers of people and mounting evidence of human-to-human transmission suggests that 2019-nCoV is more contagious than both SARS-CoV and MERS-CoV.[7,8] The first fatal case was reported on January 11, 2020. The massive migration of Chinese during the Chinese New Year fueled the epidemic. Cases in other provinces of China and those in other countries (Thailand, Japan, and South Korea in quick succession) were reported in people who were returning from Wuhan. Transmission to health-care workers caring for patients was described on January 20, 2020.

Diagnosis of COVID-19

In most cases of self-limited infection, diagnosis of coronaviruses is unnecessary, as the disease will naturally run its course. However, it may be important in certain clinical and veterinary settings or in epidemiological studies to identify an etiological agent. RT-PCR has become the method of choice for diagnosis of human CoV, as multiplex real-time RT-PCR assays have been developed, are able to detect all four respiratory HCoVs and could be further adapted to novel CoVs. Serologic assays are important in cases where RNA may be difficult to isolate, is no longer present, and for epidemiological studies. To date, there are no anti-viral therapeutics that specifically target human coronaviruses, so treatments are only supportive. In vitro, interferons (IFNs) are only partially effective against coronaviruses.

IFNs in combination with ribavirin may have increased activity in vitro when compared to IFNs alone against some coronaviruses; however, the effectiveness of this combination in vivo requires further evaluation [coronavirus] The SARS and MERS outbreaks have stimulated research on these viruses and this research has identified a large number of suitable anti-viral targets, such as viral proteases, polymerases, and entry proteins. Significant work remains, however, to develop drugs that target these processes and are able to inhibit viral replication. Only limited options are available to prevent coronavirus infections. Vaccines have only been approved for IBV, TGEV, and Canine CoV, but these vaccines are not always used because they are either not very effective, or in some cases have been reported to be involved in the selection of novel pathogenic CoVs via recombination of circulating strains. vaccine development for coronaviruses faces many challenges. First, for mucosal infections, natural infection does not prevent subsequent infection, and so vaccines must either induce better immunity than the original virus or must at least lessen the disease incurred during a secondary infection. Second, the propensity of the viruses to recombine may pose a problem by rendering the vaccine useless and potentially increasing the evolution and diversity of the virus in the wild Finally, it has been shown in FIPV that vaccination with Spike protein leads to enhanced disease. Despite this, several strategies are being developed for vaccine development to reduce the likelihood of recombination, for instance by making large deletions in the nsp1 or E proteins, rearranging the 3′ end of the genome. modifying the TRS sequences. mutant viruses with abnormally high mutation rates that significantly attenuate the virus. Owing to the lack of effective therapeutics or vaccines, the best measures to control human coronaviruses remain a strong public health surveillance system coupled with rapid diagnostic testing and quarantine when necessary. For international outbreaks, cooperation of governmental entities, public health authorities and health care providers is critical. During veterinary outbreaks that are readily transmitted, such as PEDV, more drastic measures such as destruction of entire herds of pigs may be necessary to prevent transmission of these deadly viruses.[9]

Common symptoms of COVID-19 include

Cold- or flu-like symptoms usually set in from 2–14 days after a coronavirus infection and are typically mild. However, symptoms vary from person-to-person, and some forms of the virus can be fatal.

1. Fever
2. Breathlessness

3. Sore Throat
4. Cough
5. Exacerbated asthma
6. Watery Diarrhoea
7. Running nose
8. Loss of smell and taste

Therapeutics of COVID-19

The treatment of COVID-19 is a major challenge for medical staff because there is no consensus on the optimal therapy. The evidence-based supportive care supplemented by diverse combinations of drugs is the mainstay for the management of COVID-19. In this section, we mainly summarized the clinical application of non-steroid anti-inflammatory drugs and antiviral agents. Corticosteroids were widely used in confirmed patients at the initial stage of SARS-CoV-2 outbreak, but current guidance from WHO advises against the use of corticosteroids for COVID-19.[10] Russell et al[11] explained that corticosteroids might not only prevent pulmonary progressive fibrosis and inhibit inflammatory storm, but also inhibit immune responses and subsequent pathogen clearance. Besides, lessons from managing SARS-CoV and MERS-CoV prevalence revealed that corticosteroids application is significantly correlated with adverse outcomes, including higher plasma viral load, psychosis and viremia.[12,13] However, some randomized clinical trials demonstrated that corticosteroids at low-to-moderate dose were found to reduce the duration of exiting from ICU and mechanical ventilation for critically ill patients.[14] Therefore, the guidance from Peking Union Medical College Hospital recommended systematic corticosteroids treatment (methylprednisolone, <1-2 mg/kg.d, for 3-5 days) as adjuvant therapy for individuals with rapid progression of pneumonia.[15] However, the use of corticosteroids for COVID-19 remains controversial at present, prospective randomized controlled studies are required to validate its clinical effects on COVID-19.

Specific agents of proven efficacy against SARS-CoV-2 are still being developed. Currently, there are three broad categories of antiviral agents, including immunoenhancer, spike protein-ACE2 blocker, and broad-spectrum antiviral drugs. Interferon (IFN) has been approved to have significant effects on antivirus and immunoregulation. IFN-α and IFN-β could inhibit the replication of animal and human coronaviruses[16,17], but IFN-γ did not possess antiviral activity.[18] Furthermore, IFN-α in combination with corticosteroids was reported to improve

oxygenation and faster resolution of chest radiograph abnormalities.[19] Since ACE2 is the sole receptor for spike protein of SARS-CoV-2, blocking spike protein binding to ACE2 is a key target for antivirals. Human monoclonal antibodies elicited by active or passive immunization using vaccines or convalescent plasma, is a promising blocker.[20] However ICMR studies studies have not found it worth. Though convalescent plasma is significantly associated with improved mortality, the bulk of factors limited its wide use, including the potential contamination of plasma and limited eligible donors.[21,22] Vaccines may play an important role in protecting against infection when exposed to the specific pathogen of interest, whereas there are still no commercial vaccines available against SARS-CoV-2.[23] Chloroquine as a known antima- larial drug was also found to be a potent inhibitor of SARS-CoV through interfering with ACE2.[24] A latest trial also demonstrated that chloroquine at low-micromolar concentration could block SARS- CoV-2 infection and was significantly correlated with improved clinical outcomes and shorten hospital stay.[25] As a known inhibitor of HIV cytochrome P450, the combination of lopinavir with ritonavir was found to be associated with better outcomes of COVID-19.[26,27] Moreover, the triple combination therapy of LPV/RTV, ribavirin and IFNα was recommended as an option at early stage of the disease.[28]

In addition, the limited but emerging evidence regarding expanded umbilical cord mesenchymal stem cells in managing COVID-19 suggested that it might be considered for compassionate use in critically ill patients to reduce morbidity and mortality in the United States.[29] Hypertension is one of the most frequent complications in patients with COVID-19.[30,31] Anti-hypertensive drugs (such as ACE2 inhibitors and angiotensin II receptor blockers) could increase the expression of ACE2 in some cells (particularly alveoli)[32,33], which may raise the risk of infection with SARS- CoV-2. However, scientific foundation of this theory is very weak to date.[34] Besides, the abrupt drop-out of anti-hypertensive treatment could be associated with serious risks such as acute myocardial infarction and death from cardiovascular causes.[35] There are currently more than 50 COVID-19 vaccine candidates in trials. WHO is working in collaboration with scientists, business, and global health organizations through the ACT Accelerator to speed up the pandemic response. When a safe and effective vaccine is found, **COVAX** (led by WHO, GAVI and CEPI) will facilitate the equitable access and distribution of these vaccines to protect people in all countries.[36] People with vulnerability and more risk will be prioritized. While we work towards rolling out a safe and effective vaccine fairly, we must continue the essential public health actions to suppress transmission and reduce mortality.

CONCLUSION

There are currently over 1,565,292 deaths out of more than 68,659,920 cases from 213 countries/locations globally, with India having 9,735,975 cases with 141,398 mortality till 8th December 2020. The novel virus whole-genome sequence showed 96.2% similarity to a bat SARS-related coronavirus isolated in China against <80% to the genomes of SARS-CoV and <50% to MERS-CoV. Therefore, the 2019-nCoV can be considered as a SARS-like virus, hence the name SARS-CoV-2 designated by the Coronavirus Study Group of the International Committee on Taxonomy of Viruses. However, the first preventive strategy is to interrupt the chain of transmission from animal-to-human. Understanding the epidemiology, potential pathogenesis, rapid diagnostics and effective therapeutics is crucial to SARS-CoV-2 surveillance and control. Although tremendous progress has been achieved, the continuous evolution of this RNA virus may exert new challenges on the diagnosis and treatment of COVID-19. Therefore, a larger set of prospective randomized controlled trials and basic researches is required to have a better understanding of COVID-19. Due to the rapidly evolving situation of the SARS-CoV-2, this study's limitations deserve commentary. First, there might be some bias and errors in epidemiological data as a result of many social and personal factors. Second, a proportion of evidence in our review from preprints in medRxiv and bioRxiv have not been peer reviewed. As a result, the reliability of the content in these studies needs to be further validated. Third, quality assessment and meta-analysis is not feasible due to the limited data and heterogeneous style of the recruited studies. The result of an extraordinary and unique global collaboration, with more than two-thirds of the world engaged – COVAX has the world's largest and most diverse portfolio of COVID-19 vaccines, and as such represents the world's best hope of bringing the acute phase of this pandemic to a swift end.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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