Review Article

COVID-19: global level very high risk pandemic

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ABSTRACT

Rapid worldwide spread of coronavirus disease 2019 (COVID-19) has resulted in a global pandemic. The Middle East respiratory syndrome coronavirus (MERS-CoV) was attracted a great international attention due to multiple healthcare associated outbreaks in 2012. The disease is associated with a high case fatality rate of 34.5%, and there is no recommended therapy for it. The current COVID-19 pneumonia pandemic, caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) viruses, is spreading globally at an accelerated rate. The World Health Organization declared COVID-19, a serious public health emergency, of international concern. The present article represents the epidemiology, transmissibility and treatment thought for COVID-19 disease.

Keywords: SARS-CoV, MERS-CoV, COVID-19, Pandemic, Treatment, Diagnosis

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory illness which can spread from person to person. The virus that causes COVID-19 is a novel coronavirus. It was first identified during an investigation into an outbreak in Wuhan, China.[1] Coronaviruses (CoVs) affecting upper respiratory tract were first identified in humans in mid-1960.[2] In the past ten years, many new coronaviruses have been identified which infect a wide range of hosts from mammals to birds and closely related coronaviruses have been identified in distantly related animals suggesting recent interspecies jumps.[3] Ghinai et al has represented the first person-to-person transmission of COVID-19 in the United States of America (USA), including the clinical and laboratory features of both patients and the assessment and monitoring of several hundred individuals with potential exposure to severe acute respiratory syndrome 2 (SARS-CoV-2).[4] The first case of COVID-19 in the USA was reported on 21 January 2020. Risk of infection with COVID-19 is higher for people who are close contacts of someone known to have COVID-19, for example healthcare workers, or household members.

The COVID-19 virus infects people of all ages; however the evidence suggests that, the risk of severe disease gradually increases with age starting from around 40 years.[5] The time from SARS-CoV-2 negative to positive ranged from 4 to 17 days, suggesting that recovered patients still may be virus carriers and require additional round of viral detection and isolation.[6]

Coronaviruses are minute in size (65–125 nm in diameter) and contain a single-stranded ribonucleic acid (RNA) as a nucleic material, size ranging from 26 to 32 kbs in length.[7] Like Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV, COVID-19 is a beta coronavirus which is associated with an animal reservoir (e.g. bats). However an exact animal source has not been confirmed for COVID-19, many of the early cases in China were linked to a live animal and seafood market.[8] Similar to other viruses, SARS-CoV-2 has many potential natural hosts, intermediate hosts and final hosts. This poses great challenges to prevention and treatment of virus infection. Compared with SARS and MERS, this virus has high transmissibility and infectivity, despite of low mortality rate.[9]

The current pneumonia outbreak of COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been declared a pandemic by the World Health Organization (WHO) on 11 March 2020.[10,11] The Ebola virus disease (EVD) outbreak of 2014 in West Africa taught valuable lessons for emergency preparedness, personal protective equipment (PPE) use, and triage processes, and underscored the important role that emergency physicians play on the frontlines of emerging infectious diseases.[8] There is currently no vaccine to protect against COVID-19. The best way to prevent infection is to take everyday preventive actions, like avoiding close contact with people and can seek medical care to help relieve symptoms. The current diagnostic therapy founded by the China National Health Commission, laboratory examinations, including nasopharyngeal and oropharyngeal swab tests, have become a standard assessment for the diagnosis of a COVID-19 infection.[12] Araz et al represented that the COVID-19 outbreak is one of the major disruptions encountered during the last decades which is "breaking many global supply chains".[13]

CASE DEFINITIONS

Three major trajectories for COVID-19 have been described: mild disease with upper respiratory symptoms, non-severe pneumonia, and severe pneumonia complicated by acute respiratory distress syndrome (ARDS).[8] The present clinical data obtained from 31 provinces of China shows that the COVID-19 shared many clinical features with SARS-CoV. The most common symptoms are fever (87.9%), fatigue (69.6%), dry cough (67.7%) and myalgia (34.8%), and these are accompanied with rhinobyon, rhinorrhoea, pharyngalgia and diarrhea in few patients.[10,14] Some COVID-19 patients have arrhythmia, acute heart injury, impaired renal function, and abnormal liver function (50.7%) at admission.[9] However some cases are observed to be asymptomatic and only laboratory test can provide the perfect diagnosis in this situation. Therefore WHO updates the global surveillance for human infection with COVID-19 which includes case definitions stated below.

A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness of breath), and with no other etiology that fully explains the clinical presentation and a history of travel to or residence in a country/area or territory reporting local transmission of COVID-19 disease during the 14 days prior to symptom onset.

A patient with any acute respiratory illness and having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to onset of symptoms.

A patient with severe acute respiratory infection (fever and at least one sign/symptom of respiratory disease (e.g. cough, shortness breath) and requiring hospitalization and

with no other etiology that fully explains the clinical presentation.

First case of corona virus was notified as cold in 1960. According to the Canadian study 2001, approximately 500 patients were identified as flu-like system out of 17-18 cases were confirmed as infected with corona virus strain by polymerase chain reaction. Corona was treated as simple non-fatal virus till 2002.[15] Approximately 80% of infections in COVID-19 are mild or asymptomatic, 15% are severe requiring supplemental oxygen and 5% are critical requiring mechanical ventilation.[11]

TRANSMISSIBILITY

Up to 94% of COVID-19 cases were reported to originate from Hubei Province in December 2019; as of March 2020, the highest numbers of new cases are now being reported in Italy, Spain, Germany, and the United States (U.S.).[8] SARS-CoV infects humans by close person to person contact through the respiratory tract, mainly via droplet transmission. Although human intestinal cells were proved susceptible to SARS-CoV replication, the role of the intestinal tract as a portal of entry remains uncertain.[14] Depending on the large number of infected people those were exposed to the wet animal market in Wuhan city where live animals are routinely sold, it is thought that this is the likely zoonotic origin of the COVID-19. Efforts have been made to find out for a reservoir host or intermediate carriers from which the infection may have spread to humans. Initial reports identified two species of snakes that could be a possible reservoir of the COVID-19. However, there has been no consistent evidence of coronavirus reservoirs other than mammals and birds.[16]

Epidemiologically, COVID-19 is highly infectious with about 2 hours survive time in the air and the incubation period after infection is generally 4–8 days. All age groups are susceptible to the virus, of which elderly patients with comorbidities are more likely to experience severe illness.[10] From the median incubation period, COVID-19 is shorter than SARS and MERS, but the maximum latency of COVID-19 currently observed is as high as 24 days, which may increase the risk of virus transmission.[9] The reproductive number (R0) of the novel infection is estimated by World Health Organization (WHO) to range between 2 and 2.5, which is higher than SARS (1.7-1.9) and MERS (<1), suggesting that SARS-CoV-2 has a higher pandemic potential. As per the recent descriptive study made by the Chinese center for disease control and prevention (CCDC) on 44,672 individuals diagnosed with COVID-19 in China, the fatality rate of novel coronavirus infection is estimated to be 2.3, lower than SARS (9.5%) and much lower than MERS (34.4%).[17,18] In addition to this the researchers also found that, SARS-CoV-2 in the samples of stool, gastrointestinal tract, saliva and urine whereas bioinformatics evidence indicated that digestive tract might be a potential route of COVID-19 infection. Consistently, SARS-CoV-2 RNA was also detected in gastrointestinal tissues from COVID-19 patients.

Moreover, SARS-CoV-2 was detected in the tears and conjunctival secretions of COVID-19 patients.[19]

Coronavirus S protein has been reported as a significant determinant of virus entry into host cells. The envelope spike glycoprotein binds to its cellular receptor, angiotensin converting enzyme 2 (ACE2) for SARS-CoV.[20] In a rabbit model of MERS-CoV infection, MERS-CoV was detected in the lungs without significant histopathological changes and no symptoms.[20] It is also desirable to monitor farm animals and pet cats for infection with 2019-nCoV, since their ACE2 receptor responsible for 2019-nCoV binding differs in only a few amino acids from human ACE2.[21] In addition, it has been reported that the mother was diagnosed with a new type of coronavirus pneumonia, and the newborn was positive for viral nucleic acid in pharynx swabs after 30 hours of birth, suggesting that the new type of coronavirus may cause neonatal infection through mother-to-child transmission, which of course needs to be confirmed by more scientific studies.[22]

WHO and the US food and drug administration (FDA) recommended on blood safety and pointed out a theoretical risk of transmission of the SARS virus through transfusion of blood products.[23] As a matter of safety the Wuhan blood center and all blood banks in Hubei province have started to test SARS-CoV-2 RNA from blood donations since 10 February 2020.[24]

Previous studies have drafted the recommendations that coronaviruses could be efficiently inactivated using surface disinfectants with 62–71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within 1 min, but other biocidal agents such as 0.05–0.2% benzalkonium chloride or 0.02% chlorhexidine digluconate were less effective.[25] By 04 April 2020, the global death toll reached to 56,985 with 10,51,635 laboratory-confirmed cases.[26] The disease is spreading rapidly across the globe, the spread of it since 19 December to 04 April is represented in Table 1. The data represented in Table 1 shows that the infection of COVID-19 was started in 19 December with 44 confirmed cases and reached above 10,00000 cases. There is substantial growth in confirmed cases with COVID-19 as well as deaths globally every day, as represented in Figure 1 and 2. The infection of COVID-19 was started with China and now it has been spread over 203 countries/territories/area within three months (Figure 3).
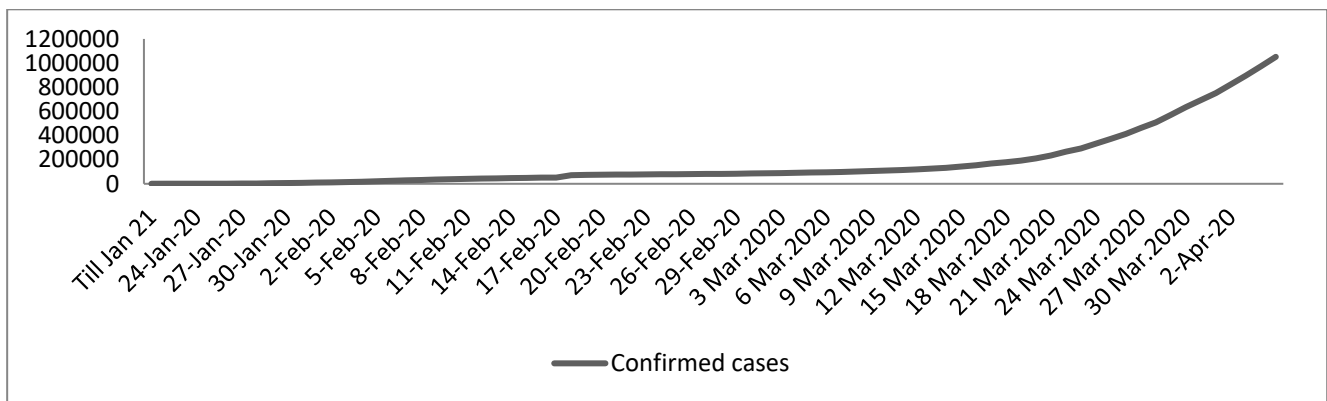
Figure 1: Reported confirmed cases of COVID-19 globally.[15,27]
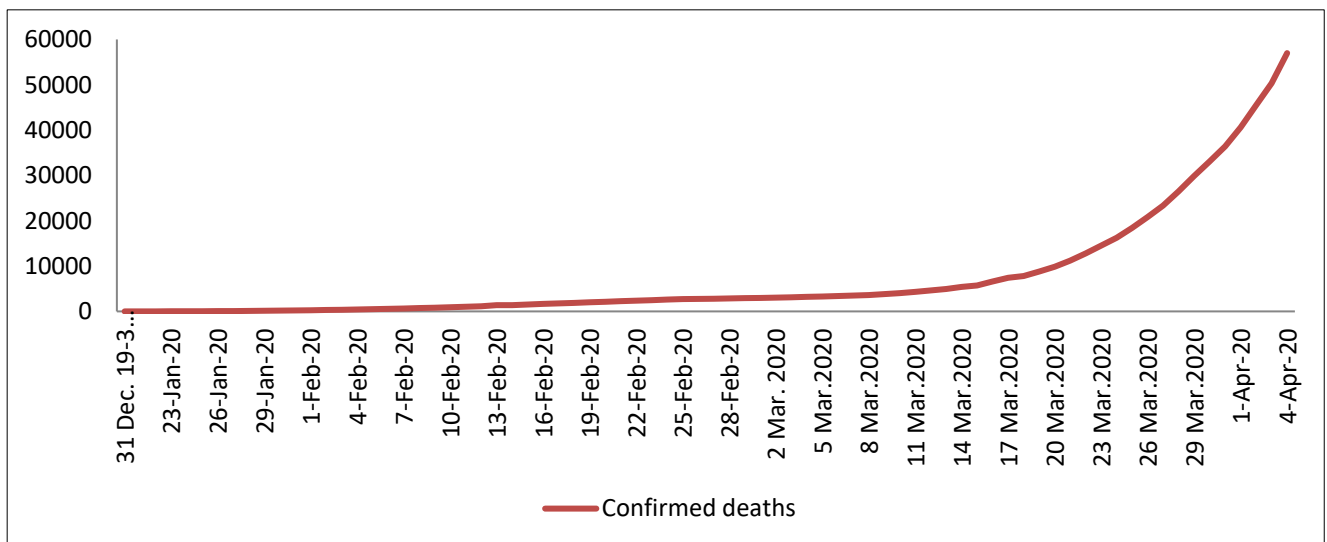
Figure 2: Reported confirmed deaths of COVID-19 globally.[15,27]
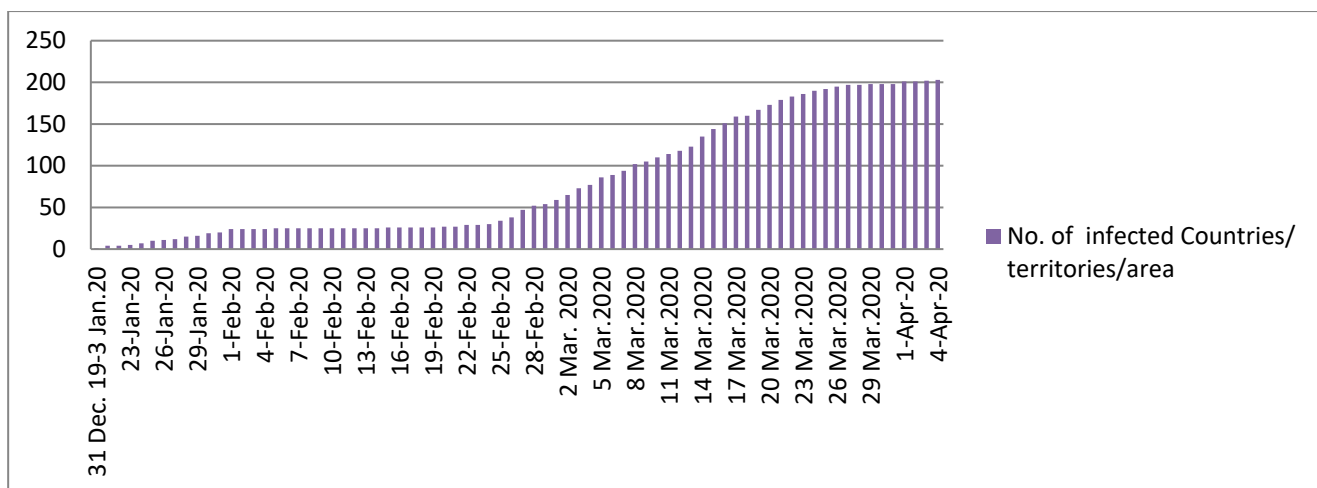
Figure 3: Countries, territories or areas with reported confirm cases of COVID-19.[15,27]

Table 1: Reported confirmed COVID-19 cases and deaths.[15,27]

Date	No. of confirmed cases	No. of new cases	No. of confirmed deaths	No. of new deaths	No. of infected countries/territ-ories/area
31 December 2019 to 03 January 2020	44	-	-	-	01
Till 21 January 2020	282	-	03	-	04
22 January 2020		32	06	03	04
23 January 2020	581	267	17	11	05
24 January 2020	846	265	25	08	07
25 January 2020	1320	471	41	16	10
26 January 2020	2014	694	56	15	11
27 January 2020	2798	784	80	24	12
28 January 2020	4593	1795	106	26	15
29 January 2020	6065	1472	132	26	16
30 January 2020	7818	1753	170	38	19
31 January 2020	9826	2008	213	43	20
1 February 2020	11953	2127	259	46	24
2 February 2020	14557	2604	304	45	24
3 February 2020	17391	2838	361	57	24
4 February 2020	20630	3241	426	65	24
5 February 2020	24554	3925	492	67	25
6 February 2020	28276	3722	565	75	25
7 February 2020	31481	3205	638	74	25
8 February 2020	34886	3419	724	87	25
9 February 2020	37558	2676	813	90	25
10 February 2020	40554	3085	910	98	25
11 February 2020	43103	2560	1018	109	25
12 February 2020	45171	2068	1115	98	25
13 February 2020	46997	1826	1369	255	25
14 February 2020	49053	2056	1383	123	25
15 February 2020	50580	1527	1526	123	26
16 February 2020	51857	1278	1669	145	26
17 February 2020	71429	2162	1775	109	26
18 February 2020	73332	1901	1873	101	26
19 February 2020	75204	1872	2009	139	26

Continued.

Date	No. of confirmed cases	No. of new cases	No. of confirmed deaths	No. of new deaths	No. of infected countries/territ-ories/area
20 February 2020	75748	548	2129	120	27
21 February 2020	76769	1021	2247	126	27
22 February 2020	77794	599	2359	112	29
23 February 2020	78811	1017	2462	103	29
24 February 2020	79331	715	2618	156	30
25 February 2020	80232	908	2700	82	34
26 February 2020	81109	871	2762	62	38
27 February 2020	82294	1185	2804	42	47
28 February 2020	83652	1358	2858	54	52
29 February 2020	85403	1753	2924	66	54
1 March 2020	87137	1739	2977	53	59
2 March 2020	88948	1806	3043	66	65
3 March 2020	90869	1922	3111	69	73
4 March 2020	93091	2223	3198	86	77
5 March 2020	95324	2232	3281	84	86
6 March 2020	98162	2873	3380	99	89
7 March 2020	101927	3735	3486	106	94
8 March 2020	105586	3656	3584	98	102
9 March 2020	109577	3993	3809	225	105
10 March 2020	113702	4125	4012	203	110
11 March 2020	118319	4620	4292	280	114
12 March 2020	125260	6741	4613	321	118
13 March 2020	132758	7499	4955	342	123
14 March 2020	142534	9764	5392	437	135
15 March 2020	153517	10982	5735	343	144
16 March 2020	167515	13903	6606	862	151
17 March 2020	179111	11525	7426	475	159
18 March 2020	191127	15123	7807	786	160
19 March 2020	209839	16556	8778	828	167
20 March 2020	234073	24247	9840	1061	173
21 March 2020	266073	32000	11183	1343	179
22 March 2020	292142	26069	12783	1600	183
23 March 2020	332930	40788	14509	1727	186
24 March 2020	372755	39825	16231	1722	190
25 March 2020	413467	40712	18433	2202	192
26 March 2020	462684	49219	20834	2401	195
27 March 2020	509164	46484	23335	2501	197
28 March 2020	571659	62495	26493	3158	197
29 March 2020	634813	63160	29891	3398	198
30 March 2020	693224	58411	33106	3215	198
31 March 2020	750890	57610	36405	3301	198
1 April 2020	823626	72736	40598	4193	201
2 April 2020	896450	72839	45526	4924	201
3 April 2020	972303	75853	50322	4823	202
4 April 2020	1051635	79332	56985	6664	203

TREATMENT AND DIAGNOSIS

An emergency medicine approach to COVID-19 should focus on identifying and isolating patients at risk for infection.[28] On COVID-19 infected patients, several therapeutic options have been experimented but still there are no specific therapies. COVID-19 is a one kind of RNA virus which may possess some similar functional proteins for processing virus replication and assembly to human immunodeficiency virus (HIV). Thus, the HIV protease inhibitors may also effective to 2019-nCov.[10]

At present, there are no specific antiviral drugs or vaccine against COVID-19 infection, the only option available is

using broad-spectrum antiviral drugs like nucleoside analogues. The treatments that have so far been attempted for 75 patients those were administrated existing antiviral drugs. The course of treatment was included twice a day oral administration of 75 mg oseltamivir, 500 mg lopinavir, 500 mg ritonavir and the intravenous administration of 0.25 g ganciclovir for 3–14 days.[29] Teicoplanin, a glycopeptide antibiotic routinely used to treat bacterial infections, was found to be active in vitro against SARS-CoV and has joined the list of molecules that could be used in the therapeutic arsenal against COVID-19.[30]

Arbidol, a small indole derivative molecule, was found suitable to block viral fusion against influenza A, B viruses and hepatitis C viruses. It was confirmed to have antiviral effect on SARS-CoV in cell experiment, so that it might be a choice for COVID-19 treatment.[31]

Moreover, thymosin alpha-1 (Ta1) can be an immune booster for SARS patients, effectively controlling the spread of disease. Intravenous immunoglobulin and Ta1 may also be considered as therapeutics for COVID-19.[31]

Many drugs have been tried recently in the treatment of COVID-19 that includes chloroquine phosphate which demonstrated marked efficacy and acceptable safety in treating COVID-19 associated pneumonia in multi-center clinical trials conducted in China.[32]

The most widely used combination is ribavirin and IFN.[34,29] In order to prevent susceptibility of lower respiratory tract infection under certain condition, a moderate amount of vitamin C supplementation may be a way to prevent COVID-19.[9,34] The viral 3-chymotrypsin-like cysteine protease 4 (3CLpro) enzyme controls coronavirus replication and is essential for its life cycle. 3CLpro is a proven drug discovery target in the case of SARS-CoV and MERS-CoV.[35]

While developing new drugs, new vaccines or clinical trials of old drugs, carrying out NK cell therapy to enhance immunity are currently a very feasible strategy for the treatment and prevention of COVID-19 pneumonia.[33] The emergency committee had recommended that the spread of COVID-19 can be interrupted by early detection, isolation, prompt treatment, and the implementation of a robust system to trace contacts.[36] Regarding diagnostic testing, US-based companies such as Co-Diagnostics and the Novacyt's molecular diagnostics division primer design had launched COVID-2019 testing kits for use in the research setting. The United Kingdom (UK) government has also invested ₤20,000,000 to develop a COVID-19 vaccine.[31,36]

For the diagnosis of COVID-19, although RT-qPCR is specific, but its false-negative rate cannot be ignored which results in to the severe consequences of missed diagnosis. Therefore many clinicians proposed CT scans should be one necessary auxiliary diagnostic method because it is more sensitive. For individuals with a high clinical suspicion of SARS-CoV-2 infection with negative RT-qPCR screening, a combination of repeated RT-qPCR tests and chest CT scan may be helpful.[36] Ultrasound can also be utilized since, it is repeatable and reliable, has no radiation, and is inexpensive. Ultrasound findings depend on the stage and severity of the disease, and it cannot detect lesions deeper in the lung. Patients with COVID-19 typically demonstrate an irregular/thickened pleural line, scattered/confluent B lines, consolidations of various sizes, and both non-translobar and translobar consolidations on lung ultrasound. Pleural effusions are typically small and localized if they are present, and abnormalities are typically found in multiple lung zones.[36]

The laboratory studies showed leucopenia with leukocyte counts of 2.91×10^9 cells/l of which 70.0% were neutrophils. Additionally, a value of 16.16 mg/l of blood C-reactive protein was noted which is above the normal range (0–10 mg/l). High erythrocyte sedimentation rate and D-dimer were also observed.[37] The detection of viral nucleic acid is the standard for noninvasive diagnosis of COVID-19.[38] Furthermore, Zhang of MIT developed a test paper for rapid detection of SARS-CoV-2 in one hour by SHERLOCK technology, although the clinical verification has not been carried out yet.[39]

RECOMMENDATIONS AND ADVICE FOR THE PUBLIC

You do not belong to the area where COVID-19 is spreading not travel from infected area and not in contact with an infected patient; your risk of infection is low. It can be understood that you may feel anxious about the outbreak. Get the facts from reliable sources to help you accurately determine your risks so that you can take reasonable precautions. It is important to be informed of the situation and take appropriate measures to protect yourself and your family.[40]

If you are in an area where there are cases of COVID-19 then you may be at the risk of infection seriously. For most people, COVID-19 infection will cause mild illness however, it can make some people very ill and, in some people, it can be fatal. Older people and those with pre-existing medical conditions (such as cardiovascular disease, chronic respiratory disease or diabetes) are at risk for severe disease. Therefore, it is significantly important to enhance self-resistance. The main way to boost personal immunity is to maintain personal hygiene, a healthy lifestyle, adequate nutritional intake, adequate rest and good ventilation.[9]

The various regulatory bodies and centers for disease control and prevention (CDC) have issued preventive measures to avoid the spread of COVID-19. They recommended avoiding travel to high risk areas, contact with individuals who are symptomatic, and the consumption of meat from regions with known COVID-19 outbreak. Basic hand hygiene measures are also

recommended, including frequent hand washing and the use of PPE such as face masks, mobile app, preventative measures that can be taken, as well as a symptom checker.[31,35]

DISCUSSION

The world has experienced three major threats of highly pathogenic coronaviruses, including the emergence of SARS-CoV in 2002, MERS-CoV in 2012 and now, the outbreak of COVID-19. It has been made clear that COVID-19 is another lineage beta coronavirus and has been postulated that bat is the primary host. COVID-19 shares many features with SARS-CoV, such as epidemiology, clinical characteristics, and the entry receptor ACE2 and so on. The COVID-19 is a catastrophic pandemic which jumps unpredictably, spreads rapidly and has created a wall to public health. Although the mortality rate for COVID-19 is lower than SARS-CoV and MARS-CoV, the mortality in elder patients with chronic diseases and intensive care unit (ICU) patients, reaching 17-38% in recent reports.

Currently no promising clinical treatments or antiviral therapy or vaccine is available prevention of human coronaviruses. However, the researchers are putting their efforts together to develop efficient therapeutic strategies to cope with the novel coronaviruses. Now it has become a need to develop, human coronaviruses targeting vaccines and antiviral drugs that could be used against the current as well as future epidemics. Supportive care and prevention of complications are the main management options available to reduce the spread of COVID-19 which includes quarantine, isolation and travel restrictions. Internationally, the number of confirmed reports has continued to rise, and is currently placed at 10,51,635 laboratory-confirmed cases with over 56,985 deaths.

CONCLUSION

It is perhaps clear that quarantine alone may not be sufficient to prevent the spread of COVID-19, at the same time; wild animals trafficking must be banned. The global impact of this viral infection is one of heightening concern.

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