

Review Article: COVID-19 Pandemic: Management and Challenges



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Article info:

Received: 19 Aug 2020

Accepted: 16 Jan 2021

Keywords:

COVID-19 Pharmacotherapy,
Prevalence, Diagnosis,
Management

ABSTRACT

Background: Coronavirus Disease 2019 (COVID-19) is an ongoing pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The outbreak was first identified in Wuhan, China, in December 2019.

Objectives: This review gives a bird's-eye view of the COVID-19 pandemic and its various effects on human society. Since knowledge about this virus is rapidly evolving, readers are urged to update themselves regularly.

Methods: In this review, our searching was performed on international databases of Embase, ScienceDirect, Scopus, PubMed, and Web of Science (ISI) from October 2019 to June 2020.

Results: Most patients infected with COVID-19 have mild symptoms. Approximately 15% of patients have severe pneumonia, and about 5% acute distress syndrome or organ failure. In the absence of definitive treatment and vaccines, the most effective measure is to prevent infection, particularly in those at high risk of taking the severe form of the disease with adverse outcomes. Pharmacotherapy is essentially supportive; the role of antiviral agents is yet to be established. The commonest drugs used in treating this viral disease are tocilizumab, remdesivir, favipiravir, and camostat mesilate. Also, drugs related to malaria, AIDS, and Ebola, such as hydroxychloroquine, are widely used. Based on physical examinations alone, it is impossible to comment with certainty in mild cases of the disease. Accordingly, a wide range of methods is used for diagnosing and treating the disease. Various variables in reducing the severity of the epidemic and the effects of the virus require special management at the national, regional, and global levels.

Conclusion: This review summarizes the latest findings in safety, management, and public services related to the COVID-19 virus epidemic.

Citation Saberi-Hasanabadi P & Mohammadi H. COVID-19 Pandemic: Management and Challenges. Pharmaceutical and Biomedical Research. 2021; 7(2):67-78. <http://dx.doi.org/10.18502/pbr.v7i2.7359>

<http://dx.doi.org/10.18502/pbr.v7i2.7359>

Introduction

In December 2019, a new human coronavirus (SARS-CoV-2) type emerged in Wuhan City, Hubei Province, China. Coronavirus disease-2019 caused by SARS-CoV-2 is now a pandemic affecting many countries. Patients with confirmed COVID-19 infection have reportedly had mild to severe respiratory illness with symptoms of cough and shortness of breath, along with other symptoms, appearing anywhere from 2 to 14 days after exposure. Older adults and people who have severe underlying medical conditions like heart or lung disease or diabetes seem to be at higher risk for developing more serious complications from COVID-19 illness [1-3]. When the body is exposed to COVID-19 infection, it becomes very severe due to the body's immune system fighting the virus. Inflammatory reactions in some people are so severe that they eventually develop pulmonary fibrosis. COVID-19 also causes severe stress on the heart [4, 5].

Clinical, laboratory, and radiological characteristics of patients indicate that COVID-19 leads to severe respiratory illness such as SARS. In sensitive groups, unlike the elderly and patients with acute underlying problems, there is currently no evidence that pregnant women are more likely to develop COVID-19 [6]. In the absence of specific pharmacotherapy treatments, complementary and alternative methods to prevent the disease are updated. Following a healthy and balanced diet with the essential nutrients can be a great way to stay healthy during the corona outbreak [7]. Although there may be good progress in medicine for the treatment of patients, efforts to reach the coronavirus vaccine will probably take time [8]. The usual drugs used in the treatment of this viral disease are tocilizumab, remdesivir, Favipiravir, camostat mesilate, and drugs related to malaria, AIDS, Ebola, such as hydroxychloroquine [9-12].

As mentioned, coronavirus disease 2019 is a pandemic influencing the first half of the year 2020. In the field of social and economic circumstances, the vulnerability of existing macroeconomics puts emerging markets and developing economies under economic and financial pressures and may limit the capacity and effectiveness of political support when the greatest need arises. The corona epidemic has disrupted two key fundamental elements: the global economy and security. The shaking of these two pillars can directly affect the future formation of the global order [13]. In countries with consumer economies, the corona viruses' crisis has provided an opportunity for the government to save resources. For this

reason, the situation is not that these societies have only suffered from this crisis. In the context of the COVID-19 virus epidemic, widespread economic crises, through less investment and innovation, the erosion of human capital due to unemployment, and the abandonment of global trade links and reserves, will impose lasting damage on potential returns. This review summarizes the latest findings in safety, management, and public services related to the COVID-19 virus epidemic.

Materials and Methods

In this review, our searching was performed on the international databases of Embase, ScienceDirect, Scopus, PubMed, and Web of Science (ISI) from October 2019 to June 2020.

Results and Discussion

Viral structure and life cycle

Coronaviruses constitute the subfamily orthocoronavirinae, in the family coronaviridae, order nidovirales, and realm riboviria (Figure 1). They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. SARS-CoV-2 enters host cells through an interaction between its "S protein" and a protein on the host cell's surface called Angiotensin-converting Enzyme 2 (ACE2). This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus [14, 15].

Genome

Coronaviruses contain a positive-sense, single-stranded RNA genome. The genome size for coronaviruses ranges from 26.4 to 31.7 kb. The number of accessory proteins and their function is unique depending on the specific coronavirus (Figure 2) [17].

Epidemiology

People of all ages can get the disease [18]. The virus that causes COVID-19 is spreading very easily and sustainably between people. Information from the ongoing COVID-19 pandemic suggests that this virus is spreading more efficiently than influenza, but not as efficiently as measles, which is highly contagious. As of June 2, 2020, 6366176 diagnosed cases of novel coronavirus pneumonia and 377437 deaths (mortality rate: 11.5%) have been reported in 213 regions or countries worldwide (Figure 3) [18]. Mortality in China and the world were almost similar for the first 20 days. There have been three high mor-

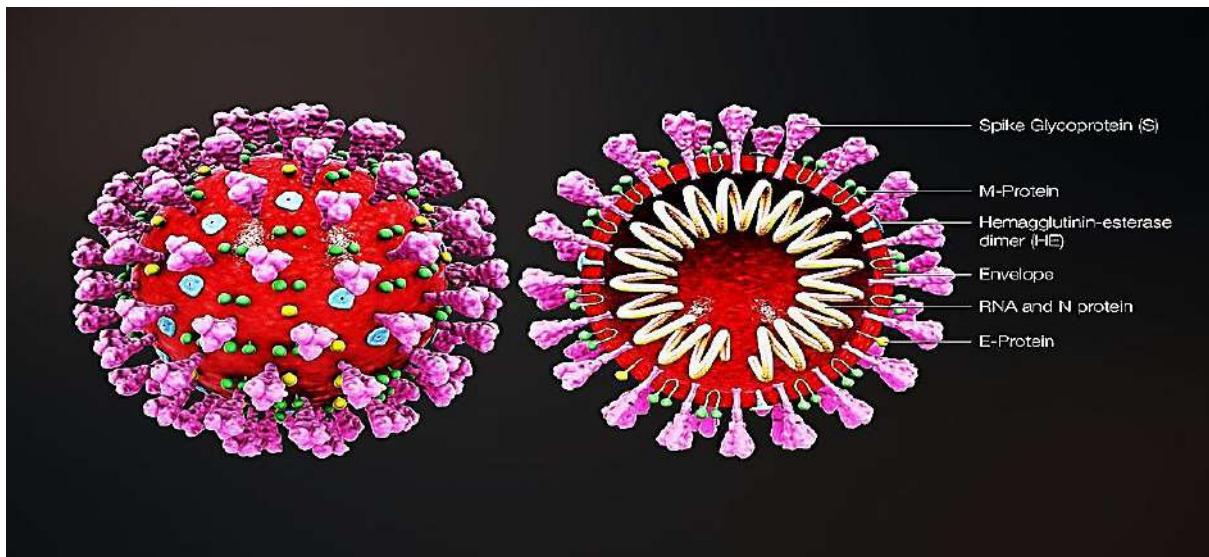


Figure 1. Cross-sectional model of a coronavirus [16]

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tality rates in Iran so far, which may be altered, and the virus mutation may be related to pathogenicity. In this regard, some reports showed that the mortality rate jumped remarkably, with an estimation of almost more than 200 deaths per day. COVID-19 that has spread around the world in recent months was the B coronavirus. The mutated virus is now known as the G-type coronavirus, which can infect many more, and if one person carries it in a group, s/he can infect many [19].

Identify and diagnose

After successful virus isolation and sequencing of the SARS-CoV-2 genome, the current diagnosis of the virus is essentially dependent on the quantitative reverse

transcription-polymerase chain reaction to identify its nucleic acid [20]. The new coronavirus is very similar to the SARS-CoV-2 known in respiratory or blood samples and can be used as a standard tool for diagnosing SARS-CoV-2 infections. Recently researchers could see the successful development of IgG and IgM antibody detection and SARS-CoV-2 antigen detectors, which have been successful in helping diagnose the virus [21, 22]. The researchers looked at more than 5300 complete genomes of the virus from 62 countries and found several mutated viruses that were “well adapted to humans”. Virus mutations are not uncommon, but researchers are concerned that COVID-19 mutations could give the virus a higher hand because it has occurred independently in 62 differ-

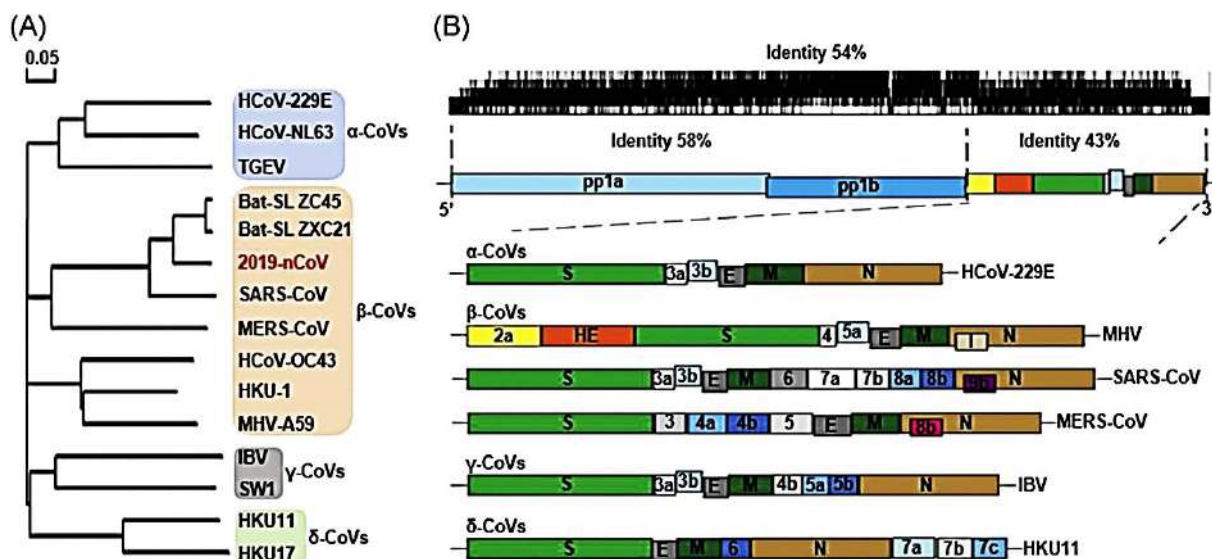


Figure 2. The genomic structure and phylogenetic tree of coronaviruses [17]

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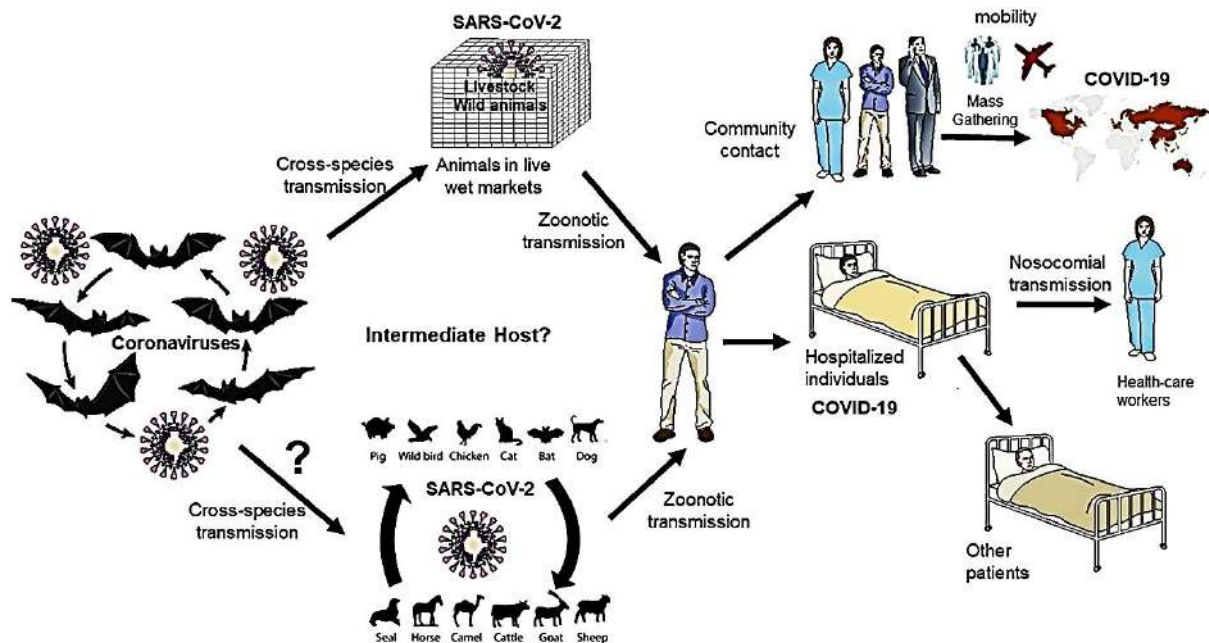


Figure 3. Generalized route of transmission of the epidemic zoonotic COVID-19 [19]

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ent countries [23]. This condition may affect the process of diagnosis, treatment, and vaccination.

Clinical characteristics

The clinical features of COVID-19 are highly variable, ranging from mild symptoms to acute respiratory syndrome and dysfunction of several internal organs. The typical clinical features include fever (not in all), cough, sore throat, headache, fatigue, myalgia, and breathlessness. Conjunctivitis has also been reported in some cases [24]. Therefore, this disease is very similar to other respiratory infections. The mortality rate in studies performed on high-risk groups (old age, diabetes, immunosuppression, etc.) varies from 10% to 60%. Clinical experience shows a meager infection rate in children compared to their adult counterparts [25]. Therefore, population groups are all at risk for the disease. According to the studied sources, the most common clinical symptoms related to COVID-19 patients were fever, non-productive cough, and shortness of breath. But a significant number of patients may seek health care without these complaints. For asymptomatic patients and those with only gastrointestinal and neurological symptoms, physicians struggle with a significant challenge [25].

Prevention, treatment, and control of COVID-19

The basic principles of prevention and control of infectious diseases include eliminating the source of the

infection, cutting off the transmission chain, and protecting the susceptible population [26]. SARS-CoV-2 is transmitted mainly through respiratory droplets and contact. Essential personal safety measures help control the spread of the virus. Vaccination is also an effective measure to protect susceptible populations. No effective vaccine has been proposed to counteract COVID-19, but several research institutes have developed SARS-CoV-2 vaccines in various ways, including mRNA-based nanotechnology and recombinant or inactive vaccine technology which has not yet been approved by the World Health Organization (WHO) [27]. So far, 165 vaccines have been developed, of which 27 entered the clinical stage, and seven entered the third clinical stage. World experience has shown that only 10% of vaccines that enter the third clinical phase will be successful. The average time it takes to make a vaccine in the last few decades has been seven years. The fact that it is now being announced that the corona vaccine can be produced for two years is such that some safety cases are considered an emergency and rejected. The Food and Drug Administration (FDA) and Centers for Disease Control (CDC) now accept a vaccine that is effective in 50% of people. There are two significant dangers to rushing to make a corona vaccine: first of all, one year or a year and a half after vaccination, strange and unknown symptoms may appear in the body because it has not been tested for a long time. Second, if we are in a hurry, it is not clear how long the body will be immune to the virus.

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Table 1. Some of the drugs, along with the reference used for COVID-19 virus treatments

Title	Dose of These Drugs	Some Clinical Trials	Ref
Chloroquine	The first dose of chloroquine is 1g × 2 days, then 0.5g × 12 days	Chloroquine seems to be effective in limiting the replication of SARS-CoV-2 (the virus causing COVID-19) in vitro studies	[36-38]
Remdesivir	200 mg intravenously on day 1, plus 100 mg daily for the following 9 days	Clinical improvement was observed in an average of more than 50% of patients	[34, 37-40]
HIV drugs	>8000 ng/mL	In mechanically ventilated patients with severe COVID-19 infections, the oral administration of lopinavir/ritonavir elicited plasma exposure of lopinavir more than 6-fold the upper usual expected range	[41, 42]
Tocilizumab	40 mg	Findings supported the effectiveness of TCZ in the prevention or treatment of cytokine storms induced by COVID-19	[43, 44]

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CT scan and COVID-19

Today, the first step in dealing with the emerging virus that travels worldwide is early detection. Some patients may be diagnosed with nasal and throat swabs or CT scans to protect the disease [28]. By comparing CT scans of previous and current patients, radiologists are aware of the effects of the virus on their lungs. Lung CT scans have become essential in rapid diagnosis and clinical decision making [29]. However, CT scans as the only way to diagnose COVID-19 may be unable to diagnose the disease early due to the similarities with the radiological findings of other lung infections [30].

Clinical treatment of COVID-19

At present, symptomatic and supportive therapies are mainly used for patients with COVID-19. These include treating underlying diseases, relieving symptoms, adequate protection and supportive care of internal organs, prevention and active treatment of secondary diseases, and, if necessary, provision of respiratory support [30]. In this regard, attention to issues such as maintaining water balance, electrolytes, and the stability of the internal matrix of the body requires more extensive measures [31].

Antiviral treatment

There are no approved drug treatments for COVID-19. However, the most effective research strategy in this situation is “old medicine, new use” (Table 1).

Remdesivir, also known by the drug code GS-5734, is a nucleoside analog drug with antiviral use and can inhibit Ebolavirus. Findings obtained from in vitro and in vivo experiments have shown that the low dose of this drug has been successful in inhibiting SARS-CoV and MERS-CoV virus strains and shown good inhibitory properties. Remdesivir can be expected to be used as one of the effective drug treatments of pulmonary infections caused by SARS-CoV-2, with positive pharmacokinetic

results and adequate immunity [32, 33]. A particular drug may be effective at one stage, but not for all situations. Remdesivir is only for patients with acute conditions, severe shortness of breath, and those who have suffered from oxygen deprivation and lung involvement and are hospitalized. Therefore, patients with mild symptoms should only rest at home and recover without taking any medication [34, 35].

As shown in laboratory tests (viruses in test tubes only), chloroquine reduces the spread and reproduction of other types of coronaviruses; however, tests on animals have proved unsuccessful [36].

The WHO is fast-tracking research into some HIV drugs like ritonavir and lopinavir, which have not shown promising results so far in smaller studies. These drugs work by blocking enzymes inside the virus and reducing its capacity to invade human cells and replicate [41].

In March 2020, China approved tocilizumab for the treatment of inflammation in patients with the coronavirus SARS-CoV-2. As of June 2020, there is no evidence of whether this treatment is effective. Additional research has shown that the administration of tocilizumab has played an essential role in preventing severe and abnormal reactions of the immune system called “cytokine storm” in some very ill patients and has prevented the deterioration of patients and even their death (Table 1) [44].

Plasma injection and Intravenous immunoglobulin (IVIg) therapy

The goal of plasma therapy is to inject plasma containing antiviral antibodies into a patient who has not responded to common medications [45]. Transfer of blood products from recovering individuals may reduce up to 50% the mortality rate of patients who have been severely affected. This approach is based on the idea that antibodies or antibodies produced by improved patients may boost the immune system of new patients. This pro-

cedure should be done at the right time because it blocks the virus and helps the new patient's immune system in time. But the time used must be carefully chosen; otherwise, it was not always successful [46].

COVID-19 and specific patients

People with certain conditions, such as diabetes, heart, or autoimmune diseases, are more likely to get coronavirus. However, the health recommendations for preventing the virus are the same for everyone.

COVID-19 and cancer patients

The risk of infection with COVID-19 is more common in certain cancer patients than in others. There are unique recommendations for patients who have undergone chemotherapy in previous years and are currently treated with a periodic examination. Patients who have had cancer-related surgery, such as breast and stomach cancer, can have chemotherapy delayed for three to four weeks and will not cause any problems. Patients currently undergoing chemotherapy have severe immunodeficiency and must be fully quarantined at home and even in a well-ventilated room with limited contact with family members [47, 48].

COVID-19 and diabetes

Briefly, people with diabetes should take the following recommendations seriously during the COVID-19 pandemic:

- Properly control their blood sugar.
- Observe a varied and balanced diet.
- Avoid stress and use relaxation techniques.
- Have enough sleep.
- Follow health advice related to corona [49].

The following results were expressed in a comprehensive review by Hussain et al. entitled "COVID-19 and diabetes: knowledge in progress". Studies have found no evidence to support the claim that Angiotensin-Converting Enzyme Inhibitors (ACEIs), angiotensin receptor blockers, or thiazolidinediones are absent in people with diabetes due to COVID-19. Caution should be taken to potential hypoglycemic events with the use of chloroquine in these subjects. Appropriate treatment strategies for people with diabetes, as stated, include careful moni-

toring of glucose levels and attention to drug interactions to reduce adverse outcomes [50].

Heart and autoimmune diseases

In short, our reviews confirmed that underlying cardiovascular disease is associated with an increased risk of in-hospital death among patients hospitalized with COVID-19. For example, in Brazil, there is a high prevalence of comorbidities (83%) among patients who died from COVID-19, with heart disease being the most prevalent. This condition is essential considering the possible secondary effects produced by drugs such as hydroxychloroquine [51]. At present, immunomodulatory drugs may be the most likely best candidates for COVID-19 therapy. There is much to learn about the interplay between infections, autoimmune diseases, and immune therapies. Leveraging knowledge of the innate and adaptive immune system will be critical as we navigate these challenging times. Rheumatologists and infectious disease specialists should be working together in this epidemic as precise data are not available, thus making recommendations speculative [52].

COVID-19 and nutrition

Some vitamins and minerals play an essential role in improving the function of the immune system, but arbitrary use of supplements containing these micronutrients can disrupt the body's normal function. Therefore, it is recommended that if a person does not have a deficiency in the absorption of micronutrients, it is better to get them through the usual food sources and avoid taking supplements without consulting a nutritionist [7]. A varied and balanced diet with an abundance of fruits and vegetables and essential nutrients like vitamin D, vitamin A, vitamin Bs (folate, vitamin B6, and vitamin B12), vitamin C, and the minerals, such as Fe, Cu, Se, and Zn well contribute to the normal functions of the immune system which may eventually accelerate the body's recovery from the disease. In both normal and emergencies, balance and variety of foods need to be regulated. Studies have shown that taking large amounts of dietary supplements does not affect the healing process of COVID-19 infection [53].

COVID-19 pandemic and global management

The outbreak of COVID-19 has shown that different parts of the global health system need to be strengthened to combat the disease spread. Countries like Singapore, Japan, and South Korea had good health and primary care systems to combat the epidemic [12, 54, 55]. We

Table 2. Some challenges in the clinical management of coronavirus disease 2019

No.	Key Conclusion	Ref
1	Ongoing clinical trials for managing the COVID-19 pandemic: it is imperative to invest international resources into high-quality design clinical trials with robust scientific rationale and vigorous statistical rigor.	[26]
2	Characteristics of and essential lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention: The global society is more interconnected than ever, and emerging pathogens do not respect geopolitical boundaries.	[54]
3	Assessment of risk factors for Coronavirus Disease 2019 (COVID-19) in health workers: Protocol for a case-control study.	[62]
4	Managing COVID-19 in surgical systems. <i>Annals of Surgery</i> : We can benefit from some of the lessons provided by our colleagues around the world to help us stay on top of these issues as we plan our approach to surgery during the pandemic.	[63]
5	Coronavirus Disease 2019 (COVID-19): A perspective from China: This review focuses on the etiology, epidemiology, and clinical symptoms of COVID-19 while highlighting the role of chest CT in prevention and disease control.	[5]
6	Consensus for prevention and management of Coronavirus Disease 2019 (COVID-19) for neurologists. <i>Stroke and Vascular Neurology</i> .	[64]

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will have problems where there is no coordination between the different health departments and the referral system is not well implemented. Human resource protection is in the guidelines of all countries.

One of the most important things besides protection is scientific advancement and attention to human resources. International cooperation should be used more effectively to prepare and distribute health items and their therapeutic experiences [56]. In the following, we briefly describe the experience of the three leading countries in the management and provision of medical services during the outbreak of COVID-19 disease.

In China, diagnostic kits were mass-produced 16 days from the start of the epidemic. In this country, rapid detection, reporting and isolation, and immediate treatment were at the top of the executive agenda. Support for the executive system in China was effective and coordinated, and at the same time as providing health care. Of course, traditional medicine is also prevalent in China. Traditional medicine was harmonized with modern medicine in this country [56, 57].

South Korea was one of the countries that paid special attention to the primary health care system. They could implement it by using timely screening and the communication mechanism between primary care and hospitals. Patients were grouped in South Korea. This grouping doesn't make much sense to people, but it can be a little painful. People's participation in South Korea was significant, and all the news was shared with the people, and justice was given to accessing the tests in South Korea [58, 59].

In Singapore, an application was developed that allowed patients to report their condition at home after they were discharged from the hospital while they were still

sick. Even if they left the house, the authorities would find out through the application. The management of private hospitals in Singapore was well-considered [60, 61]. Table 2 shows some of the latest research in the field of coronavirus disease 2019 pandemic management.

COVID-19 and hospital management

Because of the rapid spread of the disease and the lack of access to specific vaccines and drugs, hospital staff should be equipped with protective items and keep a safe distance from patients and people suspected of the corona. Depending on the number of staff and hospitalized patients, the separation of departments and individuals must be done properly. Prescribing and using the right combination of drugs will increase the quality of services provided to patients. This issue is one of the most effective factors in resource management in hospitals during COVID-19 epidemics [24].

The transfer of hospital waste during COVID-19 epidemics conditions must be done properly. The development of guidelines for transmitting infectious waste in three-layer packages and its notification to the urban waste management organization should be done as soon as possible. All vehicles must be disinfected to transport hospital waste with hydrogen peroxide or another suitable disinfectant. In the face of the threat of the COVID-19 virus, access to e-health services in the areas of prevention, monitoring, diagnosis, prioritization, treatment, and follow-up should be increased [61, 65].

COVID-19 and academic activities

Reducing participation in national and international conferences, the study opportunities of faculty members and graduate students, reducing research communica-

tion, and providing materials and requirements for research are some of the most critical challenges in university management during the COVID-19 outbreak.

The valuable solutions to manage this crisis include improving the technical context and teaching tools and defining the method of virtual evaluation, increasing the knowledge of students and faculty members to make the best use of tools, and also providing online educational services by assigning an online expert in the "Education" department of each faculty and research institute [66].

COVID-19 and market management

Deficiencies in the commodity supply chain in these circumstances may disrupt market management. Therefore, continuous monitoring of the production status of enterprises is essential, especially in the case of basic and strategic goods [66]. To achieve this goal, it is necessary to set up an online and special management system in such a way that it reports the possibility of instantaneous monitoring of inventory, import need, deficit, etc., for all basic cases.

Conclusion

COVID-19 is an emerging infectious disease that has adversely affected different areas of social life. Daily lives have been profoundly changed; economies have fallen into recession, and many traditional social, economic, and public health safety networks that many people rely on in times of hardship have been put under unprecedented strain. So, a global effort is needed to discover effective treatments to control this acute respiratory illness. The outbreak of the COVID-19 virus has caused significant economic losses and negative impacts on several human activities worldwide. Crisis management of coronavirus 2019 is an important issue that can be addressed through systematic monitoring, analysis of patient locations, hospitals, and clinics, and the distribution and provision of appropriate health care to reduce its effects. Monitoring the prevalence of COVID-19 and preparing appropriate diagnostic and treatment sites requires information about the condition, its exact location, type, and the individuals involved in the crisis.

Success in controlling the prevalence of COVID-19 in affected countries depends on cases related to scattered travel around the world and public health measures, rapid clinical identification, and precise infection control in medical centers. Clinical care of COVID-19 patients should focus on early identification, immediate isolation (separation), appropriate infection prevention, and provision of optimized supportive care. Since the disease

spreads via respiratory droplets, maintaining social distance (minimum distance of 2 m) is a suitable prevention method. Maintaining proper hygiene, good eating habits, and healthy lifestyle management can indeed be helpful for the prevention of this homicidal disease until the invention of vaccines or medicines.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

We thank all staff of the Department of Pharmacy, Mazandaran University of Medical Sciences for their help.

References

- [1] Alavi-Moghaddam M. A novel Coronavirus outbreak from Wuhan City in China, rapid need for emergency departments preparedness and response: A letter to editor. *Arch Acad Emerg Med*. 2020; 8(1):e12. [DOI:10.22037/aaem.v8i1.565] [PMID] [PMCID]
- [2] Allam Z, Jones DS. On the Coronavirus (COVID-19) outbreak and the smart city network: Universal data sharing standards coupled with Artificial Intelligence (AI) to benefit urban health monitoring and management. *Healthcare (Basel)*. 2020; 8(1):46. [DOI:10.3390/healthcare8010046] [PMID] [PMCID]
- [3] Acter T, Uddin N, Das J, Akhter A, Choudhury TR, Kim S. Evolution of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) as Coronavirus Disease 2019 (COVID-19) pandemic: A global health emergency. *Sci Total Environ*. 2020; 730:138996. [DOI:10.1016/j.scitotenv.2020.138996] [PMID] [PMCID]

- [4] Al Awaidy ST, Khamis F. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Oman: Current situation and going forward. *Oman Med J.* 2019; 34(3):181-3. [DOI:10.5001/omj.2019.36] [PMID] [PMCID]
- [5] Brindle ME, Gawande A. Managing COVID-19 in surgical systems. *Ann Surg.* 2020; 272(1):e1-2. [DOI:10.1097/SLA.0000000000003923] [PMID] [PMCID]
- [6] Nikpour M, Behmanesh F, Darzipoor M, Sadeghi Haddad Zavareh M. [Pregnancy outcomes and clinical manifestations of Covid-19 in pregnant women: A narrative review (Persian)]. *J Mil Med.* 2020; 22(2):177-83. <http://militarymedj.ir/article-1-2466-en.html>
- [7] Taghdir M, Sepandi M, Abbaszadeh S, Parastouei K. [A review on some Nutrition-Based Interventions in Covid-19 (Persian)]. *J Mil Med.* 2020; 22(2):169-76. <http://militarymedj.ir/article-1-2478-en.html>
- [8] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet.* 2020; 395(10223):507-13. [DOI:10.1016/S0140-6736(20)30211-7] [PMID] [PMCID]
- [9] Cheng Y, Wong R, Soo YOY, Wong WS, Lee CK, Ng MHL, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis.* 2005; 24(1):44-6. [DOI:10.1007/s10096-004-1271-9] [PMID] [PMCID]
- [10] Duan L, Zhu G. Psychological interventions for people affected by the COVID-19 epidemic. *Lancet Psychiatry.* 2020; 7(4):300-2. [DOI:10.1016/S2215-0366(20)30073-0] [PMID] [PMCID]
- [11] Dean CL, Hooper JW, Dye JM, Zak SE, Koepsell SA, Corash L, et al. Characterization of Ebola convalescent plasma donor immune response and psoralen treated plasma in the United States. *Transfusion.* 2020; 60(5):1024-31. [DOI:10.1111/trf.15739] [PMID]
- [12] Dong L, Hu S, Gao J. Discovering drugs to treat Coronavirus disease 2019 (COVID-19). *Drug Discov Ther.* 2020; 14(1):58-60. [DOI:10.5582/ddt.2020.01012] [PMID]
- [13] Magal P, Webb G. Predicting the number of reported and unreported cases for the COVID-19 epidemic in South Korea, Italy, France and Germany. *medRxiv.* 2020. [DOI:10.1101/2020.03.21.20040154]
- [14] Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. *Methods Mol Biol.* 2015; 1282:1-23. [DOI:10.1007/978-1-4939-2438-7_1] [PMID] [PMCID]
- [15] Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drossten C, Gulyaeva AA, et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses- a statement of the Coronavirus study group. *bioRxiv.* 2020. [DOI:10.1038/s41564-020-0695-z]
- [16] Riviera Insider. Coronavirus quarantine in France [Internet]. 2020 [Updated 2020 March 18]. Available from: <https://riviera-press.fr/insider/content/coronavirus-quarantine-france>
- [17] Mousavizadeh L, Ghasemi S. Genotype and phenotype of COVID-19: Their roles in pathogenesis. *J Microbiol Immunol Infect.* 2021; 54(2):159-63. [DOI:10.1016/j.jmii.2020.03.022] [PMID] [PMCID]
- [18] Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 among children in China. *Pediatrics.* 2020; 145(6):e20200702. [DOI:10.1542/peds.2020-0702] [PMID]
- [19] Tuite AR, Bogoch II, Sherbo R, Watts A, Fisman D, Khan K. Estimation of Coronavirus Disease 2019 (COVID-19) burden and potential for international dissemination of infection from Iran. *Ann Intern Med.* 2020; 172(10):699-701. [DOI:10.7326/M20-0696] [PMID] [PMCID]
- [20] Guan WJ, Chen RC, Zhong NS. Strategies for the prevention and management of Coronavirus Disease 2019. *Eur Respir J.* 2020; 55(4):2000597. [DOI:10.1183/13993003.00597-2020] [PMID] [PMCID]
- [21] Hsu LY, Chia PY, Lim JF. The Novel Coronavirus (SARS-CoV-2) Epidemic. *Ann Acad Med Singapore.* 2020; 49(3):105-7. [DOI:10.47102/annals-acadmedsg.202051] [PMID]
- [22] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel Coronavirus in Wuhan, China. *Lancet.* 2020; 395(10223):497-506. [DOI:10.1016/S0140-6736(20)30183-5]
- [23] World Health Organization (WHO). Laboratory testing for Coronavirus Disease 2019 (COVID-19) in suspected human cases: interim guidance, March 2 2020 [Internet]. 2020 [Updated 2020 March 2]. Available from: <https://apps.who.int/iris/handle/10665/331329>
- [24] Jin H, Hong C, Chen S, Zhou Y, Wang Y, Mao L, et al. Consensus for prevention and management of Coronavirus Disease 2019 (COVID-19) for neurologists. *Stroke Vasc Neurol.* 2020; 5(2):146-51. [DOI:10.1136/svn-2020-000382] [PMID] [PMCID]
- [25] Naderpour Z, Saeedi M. A primer on COVID-19 for clinicians: Clinical manifestation and natural course. *Adv J Emerg Med.* 2020; 4(2s):e62. [DOI:10.22114/ajem.v4i2s.418]
- [26] Kahn N. New virus discovered by Chinese scientists investigating pneumonia outbreak [Internet]. 2020 [Updated 2020 January 8]. Available from: https://scholar.google.com/scholar?hl=fa&as_sdt=0%2C5&q=+New+virus+discovered+by+Chinese+scientists+investigating+pneumonia+outbreak&btnG=
- [27] Libert C, Dejager L, Pinheiro I. The X chromosome in immune functions: When a chromosome makes the difference. *Nat Rev Immunol.* 2010; 10(8):594-604. [DOI:10.1038/nri2815] [PMID]
- [28] Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl).* 2020; 133(9):1025-31. [DOI:10.1097/CM9.0000000000000744] [PMID] [PMCID]
- [29] Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT findings in Coronavirus Disease-19 (COVID-19): Relationship to duration of infection. *Radiology.* 2020; 295(3):200463. [DOI:10.1148/radiol.2020200463] [PMID] [PMCID]
- [30] Kazemina M, Jalali R, Vaisi-Raygani A, Khaledi-Paveh B, Salari N, Mohammadi M, et al. [Fever and cough are two important factors in identifying patients with the Covid-19:

- A meta-analysis (Persian)]. *J Mil Med.* 2020; 22(2):193-202. <http://militarymedj.ir/article-1-2449-en.html>
- [31] Le TT, Andreadakis Z, Kumar A, Gómez Román R, Tollefsen S, Saville M, et al. The COVID-19 vaccine development landscape. *Nat Rev Drug Discov.* 2020; 19(5):305-6. [DOI:10.1038/d41573-020-00073-5] [PMID]
- [32] Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel Coronavirus (2019-nCoV) in vitro. *Cell Res.* 2020; 30(3):269-71. [DOI:10.1038/s41422-020-0282-0] [PMID] [PMCID]
- [33] Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, et al. Remdesivir in adults with severe COVID-19: A randomised, double-blind, placebo-controlled, multicentre trial. *Lancet.* 2020; 395(10236):1569-78. [DOI:10.1016/S0140-6736(20)31022-9] [PMID] [PMCID]
- [34] Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, et al. Compassionate use of remdesivir for patients with severe Covid-19. *N Engl J Med.* 2020; 382(24):2327-36. [DOI:10.1056/NEJMoa2007016] [PMID] [PMCID]
- [35] Al-Tawfiq JA, Al-Homoud AH, Memish ZA. Remdesivir as a possible therapeutic option for the COVID-19. *Travel Med Infect Dis.* 2020; 34:101615. [DOI:10.1016/j.tmaid.2020.101615] [PMID] [PMCID]
- [36] Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J Crit Care.* 2020; 57:279-83. [DOI:10.1016/j.jcrc.2020.03.005] [PMID] [PMCID]
- [37] Sahraei Z, Shabani M, Shokouhi S, Saffaei A. Aminoquinolines against Coronavirus Disease 2019 (COVID-19): Chloroquine or hydroxychloroquine. *Int J Antimicrob Agents.* 2020; 55(4):105945. [DOI:10.1016/j.ijantimicag.2020.105945] [PMID] [PMCID]
- [38] Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents.* 2020; 55(4):105932. [DOI:10.1016/j.ijantimicag.2020.105932] [PMID] [PMCID]
- [39] Cao YC, Deng QX, Dai SX. Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. *Travel Med Infect Dis.* 2020; 35:101647. [DOI:10.1016/j.tmaid.2020.101647] [PMID] [PMCID]
- [40] Ko WC, Rolain JM, Lee NY, Chen PL, Huang CT, Lee PI, et al. Arguments in favour of remdesivir for treating SARS-CoV-2 infections. *Int J Antimicrob Agents.* 2020; 55(4):105933. [DOI:10.1016/j.ijantimicag.2020.105933] [PMID] [PMCID]
- [41] Lê MP, Jaquet P, Patrier J, Wicky PH, Le Hingrat Q, Veyrier M, et al. Pharmacokinetics of lopinavir/ritonavir oral solution to treat COVID-19 in mechanically ventilated ICU patients. *J Antimicrob Chemother.* 2020; 75(9):2657-60. [DOI:10.1093/jac/dkaa261] [PMID] [PMCID]
- [42] American Academy of Pediatrics Committee on Pediatric AIDS, Section on International Child Health, Havens PL, Gibb DM. Increasing antiretroviral drug access for children with HIV infection. *Pediatrics.* 2007; 119(4):838-45. [DOI:10.1542/peds.2007-0273] [PMID]
- [43] Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: A single center experience. *J Med Virol.* 2020; 92(7):814-8. [DOI:10.1002/jmv.25801] [PMID] [PMCID]
- [44] Fu B, Xu X, Wei H. Why tocilizumab could be an effective treatment for severe COVID-19? *J Transl Med.* 2020; 18(1):164. [DOI:10.1186/s12967-020-02339-3] [PMID] [PMCID]
- [45] Leider JP, Brunker PAR, Ness PM. Convalescent transfusion for pandemic influenza: Preparing blood banks for a new plasma product? *Transfusion.* 2010; 50(6):1384-98. [DOI:10.1111/j.1537-2995.2010.02590.x] [PMID] [PMCID]
- [46] Rubin R. Testing an old therapy against a new disease: Convalescent plasma for COVID-19. *JAMA.* 2020; 323(21):2114-17. [DOI:10.1001/jama.2020.7456] [PMID]
- [47] Burki TK. Cancer guidelines during the COVID-19 pandemic. *Lancet Oncol.* 2020; 21(5):629-30. [DOI:10.1016/S1470-2045(20)30217-5] [PMID] [PMCID]
- [48] Lythgoe MP, Middleton P. Ongoing clinical trials for the management of the COVID-19 pandemic. *Trends Pharmacol Sci.* 2020; 41(6):363-82. [DOI:10.1016/j.tips.2020.03.006] [PMID] [PMCID]
- [49] Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med.* 2020; 8(4):e21. [DOI:10.1016/S2213-2600(20)30116-8] [PMID] [PMCID]
- [50] Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. *Diabetes Res Clin Pract.* 2020; 162:108142. [DOI:10.1016/j.diabres.2020.108142] [PMID] [PMCID]
- [51] Pachiega J, Dos Santos Afonso AJ, Sinhoroim GT, de Alencar BT, de Araújo MDSM, Longhi FG, et al. Chronic heart diseases as the most prevalent comorbidities among deaths by COVID-19 in Brazil. *Rev Inst Med Trop Sao Paulo.* 2020; 62:e45. [DOI:10.1590/s1678-9946202062045] [PMID] [PMCID]
- [52] Askanase AD, Khalili L, Buyon JP. Thoughts on COVID-19 and autoimmune diseases. *Lupus Sci Med.* 2020; 7(1):e000396. [DOI:10.1136/lupus-2020-000396] [PMID] [PMCID]
- [53] Dietz W, Santos-Burgoa C. Obesity and its implications for COVID-19 mortality. *Obesity (Silver Spring).* 2020; 28(6):1005. [DOI:10.1002/oby.22818] [PMID]
- [54] Wong JEL, Leo YS, Tan CC. COVID-19 in Singapore-current experience: Critical global issues that require attention and action. *JAMA.* 2020; 323(13):1243-4. [DOI:10.1001/jama.2020.2467] [PMID]
- [55] Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA.* 2020; 323(15):1488-94. [DOI:10.1001/jama.2020.3204] [PMID] [PMCID]
- [56] Phua J, Weng L, Ling L, Egi M, Lim CM, Divatia JV, et al. Intensive care management of Coronavirus Disease 2019 (COVID-19): Challenges and recommendations. *Lancet Respir Med.* 2020; 8(5):506-17. [DOI:10.1016/S2213-2600(20)30161-2] [PMID] [PMCID]
- [57] Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. *Nature.* 2020; 579(7798):265-9. [DOI:10.1038/s41586-020-2008-3] [PMID] [PMCID]
- [58] Shim E, Tariq A, Choi W, Lee Y, Chowell G. Transmission potential and severity of COVID-19 in South Korea. *Int J Infect Dis.* 2020; 93:339-44. [DOI:10.1016/j.ijid.2020.03.031] [PMID] [PMCID]

- [59] Her M. How is COVID-19 affecting South Korea? What is our current strategy? *Disaster Med Public Health Prep.* 2020; 14(5):684-6. [DOI:10.1017/dmp.2020.69] [PMID] [PMCID]
- [60] Pung R, Chiew CJ, Young BE, Chin S, Chen MIC, Clapham HE, et al. Investigation of three clusters of COVID-19 in Singapore: Implications for surveillance and response measures. *Lancet.* 2020; 395(10229):1039-46. [DOI:10.1016/S0140-6736(20)30528-6] [PMID] [PMCID]
- [61] Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA.* 2020; 323(13):1239-42. [DOI:10.1001/jama.2020.2648] [PMID]
- [62] World Health Organization (WHO). Assessment of risk factors for Coronavirus Disease 2019 (COVID-19) in health workers: Protocol for a case-control study [Internet]. 2020 [Updated 2020 May 26]. Available from: [https://www.who.int/publications/i/item/assessment-of-risk-factors-for-coronavirus-disease-2019-\(covid-19\)-in-health-workers-protocol-for-a-case-control-study](https://www.who.int/publications/i/item/assessment-of-risk-factors-for-coronavirus-disease-2019-(covid-19)-in-health-workers-protocol-for-a-case-control-study)
- [63] Zu ZY, Jiang MD, Xu PP, Chen W, Ni QQ, Lu GM, et al. Coronavirus Disease 2019 (COVID-19): A perspective from China. *Radiology.* 2020; 296(2):E15-25. [DOI:10.1148/radiol.2020200490] [PMID] [PMCID]
- [64] Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. [Management of Coronavirus Disease-19 (COVID-19): The Zhejiang experience (Chinese)]. *Zhejiang Da Xue Xue Bao Yi Xue Ban.* 2020; 49(1):147-57. [DOI: 10.3785/j.issn.1008-9292.2020.02.02] [PMID]
- [65] Yu H, Sun X, Solvang WD, Zhao X. Reverse logistics network design for effective management of medical waste in epidemic outbreaks: Insights from the coronavirus disease 2019 (COVID-19) outbreak in Wuhan (China). *Int J Environ Res Public Health.* 2020; 17(5):1770. [DOI:10.3390/ijerph17051770] [PMID] [PMCID]
- [66] Cao W, Fang Z, Hou G, Han M, Xu X, Dong J, et al. The psychological impact of the COVID-19 epidemic on college students in China. *Psychiatry Res.* 2020; 287:112934. [DOI:10.1016/j.psychres.2020.112934] [PMID] [PMCID]

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