



Prevention, Possible Treatment and Control of Corona Virus (SARS-CoV-2)

Md. Mahmudul Islam Khan^{1*}, Lincon Chandra Shill¹, Nafisa Habib Purba²,
Moumita Chakma¹, Vulon Prosad² and Ahmedur Rahman Rumel¹

¹Noakhali Science and Technology University, Bangladesh.

²Integrated Nutrition Intervention Project, Society for Health Extension and Development (SHED),
Bangladesh.

Authors' contributions

This work was carried out in collaboration among all authors. All authors contributed equally to conceptualized the idea, read the literature, find the information on different web site and prepared the manuscript and drafting. All authors read and approved the final manuscript.

Article Information

Editor(s):

- (1) Dr. Darko Nozic, University of Belgrade, Serbia.
- (2) Dr. Cynthia Aracely Alvizo Báez, Autonomous University of Nuevo Leon, Mexico.
- (3) Dr. Jaffu Othniel Chilongola, Tumaini University, Tanzania.

Reviewers:

- (1) Mor, Darca & Bnei Akiva Schools, Israel.
 - (2) Siti Chandra Widjanantie, University of Indonesia, Indonesia.
 - (3) Pankaj Raj Nepal, FCPS, Nepal.
 - (4) Mehdi Khanbabayi Gok, Tabriz University of Medical Science, Iran.
 - (5) Mona R. Patel, Gujarat Technological University, India.
- Complete Peer review History: <http://www.sdiarticle4.com/review-history/61490>

Review Article

Received 11 September 2020

Accepted 02 October 2020

Published 27 October 2020

ABSTRACT

Present days world is facing a great challenge to stop a pandemic outbreak of Coronavirus disease 2019 (COVID-19) which is caused by SARS-CoV-2. This was first reported in Wuhan, Hubei, China in December 2019, and it spread rapidly across the world, resulting in the World Health Organization announcing a global health emergency on 30 January 2020. Currently, there is no registered treatment or vaccine for the disease. In the absence of a specific treatment for this novel virus, there is an urgent need to find an alternative solution to prevent and control the replication and spread of the virus. In this situation, we should follow some guidelines or suggestions provided by the renowned health sector such as WHO. First, to increase our immunity, we have to take nutrition supplement or foods which contain immunity enhancer vitamins and minerals. Second, to

*Corresponding author: E-mail: mikshakil@yahoo.com;

control this pandemic we should practice good personal hygiene. And if we are affected, we should take some medicine as the doctor's guideline. In this article, we summarize the possible prevention, treatment and control measures of this pandemic.

Keywords: SARS-CoV-2; prevention; control; treatment.

1. INTRODUCTION

Present days world is facing a great challenge to stop a pandemic outbreak of Coronavirus disease 2019 (COVID-19) which is caused by SARS-CoV-2 [1]. This was first reported in Wuhan, Hubei, China in December 2019, and it spread rapidly across the world, resulting in the World Health Organization announcing a global health emergency on 30 January 2020 [2]. According to WHO until 11th September 2020 COVID-19 covers 216 countries where total disease cases are 27,973,127 and total death is 905,426. Coronaviruses (CoVs) belong to the subfamily *Orthocoronavirinae* in the family of *Coronaviridae* in the order *Nidovirales*, and this subfamily including α -coronavirus, β -coronavirus, γ -coronavirus, and delta-coronavirus [3]. Coronaviruses primarily cause enzootic infections in birds and mammals and, in the last decades, have shown to be capable of infecting humans as well [4]. The outbreak of severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012 has demonstrated the lethality of coronaviruses when they cross the species barrier and infect humans [4]. SARS-CoV and MERS-CoV all belong to the β -coronavirus family [5]. Recent, coronavirus (COVID-19) related to the MERS and SARS coronaviruses was found at the end of 2019 in China and the evidence of human-to-human transmission was confirmed among close contacts [6]. The genome of COVID-19 is a single-stranded positive-sense RNA [7]. The sequence analysis showed that the COVID-19 possessed a typical genome structure of coronavirus and belonged to the cluster of β -coronaviruses including SARS-CoV and MERS-CoV [7]. COVID-19 was more than 82% identical to those of SARS-CoV [8,9]. Now COVID-19 spread worldwide with its devastating paw. Currently, there is no registered treatment or vaccine for the disease. In the absence of a specific treatment for this novel virus, there is an urgent need to find an alternative solution to prevent and control the replication and spread of the virus. We have done an online search on PubMed and Web of Science with the keywords of SARS, MERS, novel coronaviruses. We summarize the possible prevention, treatment

and control measures of this pandemic. We also try to pick some challenges to control the devastating paw of this virus.

2. PREVENTION

As there have no specific or registered treatment and vaccine and our body defensive mechanism been the only hope to prevent coronavirus disease in 2019, then we have to increase our immunity. To increase our immunity, we have to take nutrition supplement or foods which contain immunity enhancer vitamins and minerals. There are different vitamins and minerals which increase our immunity ability against different viral disease. They are discussed below:

2.1 Vitamin A

Vitamin A is a fat-soluble vitamin to be recognized and its plant-derived precursor is β -carotene. Vitamin A is also called an "anti-infective" vitamin and many of our body's defenses against infection depend on an adequate supply. Many researchers have believed that the deficiency of a particular nutritional element causes an impaired immune response [10]. Measles and diarrhea are strongly associated with Vitamin A deficiency and measles can become severe in vitamin A deficient children. In addition, Semba et al had reported that vitamin A supplementation can reduce morbidity and mortality in different infectious diseases, such as measles, diarrheal disease, measles-related pneumonia, human immunodeficiency virus (HIV) infection, and malaria [10-12]. Jee et al had reported in his article that low vitamin A diets might have the effectiveness of inactivated bovine coronavirus vaccines and render calves more susceptible to infectious disease. The effect of infection with infectious bronchitis virus (IBV), a kind of coronaviruses, was more pronounced in chickens fed a diet marginally deficient in vitamin A than in those fed a diet adequate in vitamin A [13,14]. Vitamin A and retinoids inhibit measles replication through which mechanism is upregulating elements of the innate immune response in uninfected bystander cells, making them refractory to productive infection during

subsequent rounds of viral replication [15]. Therefore, for the treatment of this novel coronavirus and the prevention of lung infection vitamin A could be a promising option. Sources of Vitamin A are highest in liver and fish oils. Other sources of vitamin A are milk and eggs, leafy green vegetables, orange and yellow vegetables, tomato, fruits, and some vegetable oils [16].

2.2 B Vitamins

B vitamins are water-soluble vitamins and work as coenzymes. Each B vitamin has a special role in our body. For example, the main role of vitamin B2 (riboflavin) is to regulate the energy metabolism of all cells [17]. Keil et al had reported that UV light and vitamin B2 effectively reduced the titer of MERS-CoV in human plasma products [18]. Vitamin B3, also known as nicotinamide, could enhance the destruction of *Staphylococcus aureus* through a myeloid-specific transcription factor [19]. Moreover, during ventilator-induced lung injury, vitamin B3 treatment significantly inhibited neutrophil infiltration into the lungs with a strong anti-inflammatory effect. Vitamin B6 is essential in protein metabolism and it participates in over 100 reactions in body tissues. In addition, B6 also plays an important role in the body's immune function. Deficiency of B vitamins may weaken the host immune response, they should be supplemented to the virus-infected patients to enhance their immune system [19,20]. Therefore, B vitamins could be chosen as a basic option for the treatment of COVID-19. The best sources of Vitamin B complex are whole grains, red meat, poultry, fish, eggs, milk, beans, seeds, nuts, different fruits, etc. [21].

2.3 Vitamin C

Vitamin C is a water-soluble vitamin and it is also known as ascorbic acid. Vitamin C is well known for its important role in the synthesis of collagen in connective tissues and also acts as an antioxidant. Vitamin C supports immune functions and protects against infection caused by a coronavirus [22]. For example, Atherton et al had reported that the resistance of chick embryo tracheal organ cultures to avian coronavirus infection is increased by Vitamin C [23]. Vitamin C also has a function as a weak antihistamine agent to give relief from flu-like symptoms such as sneezing, a running or stuffy nose, and swollen sinuses [24]. A controlled trial among three humans had reported that there

was a significantly lower incidence of pneumonia in vitamin C-supplemented groups, which suggested that vitamin C might prevent the susceptibility to lower respiratory tract infections under certain conditions [25]. However, the COVID-19 had been reported to cause lower respiratory tract infection, so vitamin C could be one of the effective choices for the treatment of COVID-19. Different Citrus fruits, tomatoes, and potatoes are major contributors to vitamin C. Other good food sources include red and green peppers, kiwifruit, broccoli, strawberries, Brussels sprouts, and cantaloupe, etc. [26].

2.4 Vitamin D

Vitamin D is an important nutrient and also acts as a hormone, which can be synthesized in our body with the help of sunlight. Maintaining bone integrity is its main role and in addition, it also stimulates the maturation of many cells including immune cells. People who are housebound, or institutionalized and those who work at night may have vitamin D deficiency, as do many elderly people, who have limited exposure to sunlight [27,28]. The COVID-19 was first identified in the Winter season of 2019 and mostly affected middle-aged to elderly people. The virus-infected people might have insufficient vitamin D. In addition, the decreased vitamin D status in calves had been reported to cause the infection of bovine coronavirus [29]. Therefore, vitamin D may be another therapeutic option for the treatment of this novel virus. The flesh of fatty fish (such as trout, salmon, tuna, and mackerel) and fish liver oils are among the best sources. Mushrooms, milk, soy, eggs, etc. also contain a certain amount of vitamin D [30].

2.5 Vitamin E

Vitamin E is a lipid-soluble vitamin. It plays an important role as an antioxidant to reduce oxidative stress through binding to free radicals [31]. Vitamin E and selenium deficiency had been reported to intensify the myocardial injury of coxsackievirus B3 infection in mice [32,33]. In addition, the decreased vitamin E and D status in calves also caused the infection of bovine coronavirus [29]. Numerous foods provide vitamin E such as nuts, seeds, and vegetable oils, corn, etc. [34].

2.6 Omega-3 Polyunsaturated Fatty Acids

Long-chain polyunsaturated fatty acids (PUFAs) are essential mediators of inflammation and adaptive immune responses. Anti-inflammatory

and pro-inflammatory effects are predominantly promoted by omega-3 and omega-6 PUFAs [35]. Begin et al had studied AIDS patient's plasma lipids levels and had found that a selective and specific lack of the long-chain PUFAs of omega-3 series, which are found in high concentrations in fish oils [36]. In addition, protectin D1, the omega-3 PUFA-derived lipid mediator, could markedly attenuate influenza virus replication via RNA export machinery. Again, mice can be rescued completely from flu mortality by the treatment of protectin D1 with peramivir [37]. Several PUFAs also had anti-hepatitis C virus (HCV) activities which were found in a study by Leu et al. [38]. Therefore, Omega-3 including protectin D1, which served as a novel antiviral drug, could be considered for one of the potential interventions of this novel virus, COVID-19. Sources of Omega-3 polyunsaturated fatty acids are plant oils, soybean, canola oils, Chia seeds, walnuts, cold-water fatty fish, such as salmon, mackerel, tuna, herring, and sardines, etc. [39].

2.7 Selenium

Selenium is an essential trace element. Oxidative stress caused in the host because of dietary selenium deficiency can alter a viral genome so that a normally benign or mildly pathogenic virus can become highly virulent in the deficient host under oxidative stress [40]. Selenium deficiency also induces not only impairment of the host immune system, but also a rapid mutation of benign variants of RNA viruses to virulence [41]. It is because selenium in concert with vitamin E could assist a group of enzymes that, work to prevent the formation of free radicals and prevent oxidative damage to cells and tissues [42]. Therefore, selenium supplementation also could be an effective choice for the treatment of this novel virus of COVID-19. Brazil nuts, seafood, and organ meats are the richest food sources of selenium. Other sources include muscle meats, eggs, cereals and other grains, and dairy products etc. [43].

2.8 Zinc

For the maintenance and development of immune cells of both the innate and adaptive immune system Zinc is an important trace mineral in our diet [44]. Zinc deficiency causes dysfunction of both humoral and cell-mediated immunity and also increases susceptibility to infectious diseases [45]. Lower respiratory tract infections cause measles-related morbidity and mortality can be reduced by given Zinc

supplementation to zinc-deficient children [46]. The replication of a variety of RNA viruses can efficiently be impaired by increasing the concentration of intracellular zinc with zinc-ionophores like pyrithione [46]. In addition, the replication of SARS coronavirus (SARS-CoV) can be inhibited by the combination of zinc and pyrithione at low concentrations [47]. Therefore, zinc supplement may have an effect not only on COVID-19-related symptoms like diarrhea and lower respiratory tract infection but also on COVID-19 itself. A wide variety of foods contain zinc, such as oysters, red meat, poultry provide the majority of zinc. Other good food sources include beans, nuts, certain types of seafood (such as crab and lobster), whole grains, dairy products, etc. [48]

2.9 Iron

Iron is another important trace element that is required for both host and pathogen. Iron deficiency can impair host immunity, while iron overload can cause oxidative stress to propagate harmful viral mutations [49]. It has been reported that iron deficiency is a risk factor for the development of recurrent acute respiratory tract infections [50]. Therefore, iron may be considered as an important mineral to enhance our immunity against COVID-19. The richest sources of iron in the diet include lean meat, seafood, nuts, beans, vegetables, and fortified grain products, etc. Breast milk contains highly bioavailable iron, but it is not sufficient to meet the needs of infants older than 4 to 6 months [51].

After all, besides the immunity-boosting we should also follow some personal hygiene regulation which we mention in the control line.

3. POSSIBLE TREATMENT

3.1 Human Monoclonal Antibody

Monoclonal antibodies targeting vulnerable sites on viral surface proteins are well recognized as a promising class of drugs against anti-infectious diseases and have demonstrated therapeutic efficacy for many viruses. [52] Coronavirus neutralizing antibodies specifically target the trimeric spike (S) glycoproteins on the viral surface that facilitate entry into host cells. The S protein has two functional subunits that mediate cell attachment (the S1 subunit, which consists of four core domains S1A through S1D) and viral and cell membrane fusion (the S2 subunit).

3.2 Chloroquine and Hydroxychloroquine

Since 1934, chloroquine is known as 9-aminoquinoline. In addition to its well-known antimalarial activity, the drug also has many important biochemical properties including antiviral effects. [53] Additionally, it was used against infection with the virus. Chloroquine was also found to be a potent inhibitor of SARS coronavirus infection by interacting with ACE2, a cell surface binding sites for spike protein of SARS-CoV. [54] According to Gautret et al. Chloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2 and reported to be efficient in Chinese COV-19 patients. [55] But recently FDA said that Hydroxychloroquine and chloroquine have not been shown to be safe and effective for treating or preventing COVID-19. They also said that Hydroxychloroquine and chloroquine can cause abnormal heart rhythms such as QT interval prolongation and ventricular tachycardia (an extremely rapid heart rate).

3.3 Emodin

Emodin is an anthraquinone equivalent derived from the genus *Rheum* and *Polygonum* and is also a virucidal agent [56]. Ho et al. reported that emodin significantly blocked the S protein and ACE2 interaction in a dose-dependent manner. It was also found to inhibit the infectivity of S protein-pseudotyped retrovirus to Vero E6 cells. These findings suggested that emodin may be considered as a possible lead therapeutic agent in SARS treatment [56].

3.4 Promazine

Antipsychotics are psychiatric medications available on prescription and are licensed to treat types of mental health disorders that include psychotic experiences in their symptoms. Promazine is a first-generation antipsychotic [57]. Promazine and emodin have a common structure. It was found to exhibit a major effect in inhibiting SARS CoV replication [58].

3.5 Nicotianamine

Nicotianamine is a vital metal-ligand in plants and found as a novel angiotensin-converting enzyme-2 inhibitor in soybean [59,60]. So, this is yet another possible way to reduce COVID-19 infection.

3.6 Ribavirin

Ribavirin is an antiviral agent that interferes with the replication of DNA and RNA viruses. The ribavirin is not only interfering with the polymerases but also interferes with RNA capping to prevent RNA degradation [61]. Ribavirin has a well-established history of usage during the outbreak of SARS [62]. COVID-19 pathology is similar to the 2003 SARS-CoV & 2013 MERS-CoV and due to this similarity previous treatment guidance can provide guidance for the current outbreak of 2019-CoV [63]. There was a report that had been mentioned that there is no significant activity against SARS-CoV *in vitro* [64]. Treatment with the combination of chloroquine and ribavirin may give some advantage in an outbreak due to immediate drug availability. There had been reported that ribavirin and interferon-beta prevented the replication of SARS-associated coronavirus in animal and human cell lines [65].

3.7 Remdesivir

Remdesivir is a prodrug of a nucleotide analog that prevents viral RNA polymerases. Remdesivir has the activity against some virus families including coronaviruses (SARS-CoV & MERS-CoV) [66]. Recently it has been found that the antiviral activity of RDV and IFN-beta showed a better result than LPV/RTV-IFN-beta against MERS-CoV *in vitro* and *in vivo* [67]. Study finds out that 68% of severe COVID-19 patient who is treated with remdesivir has shown clinical improvement [67]. Remdesivir could be a better choice in the treatment of COVID-19. To find out the efficiency and safety of remdesivir still more trials be needed.

3.8 Nelfinavir

Nelfinavir is known as a safe antiviral drug and has been a widely used inhibitor of the HIV-1 protease. It is used with the combination of other antiretroviral medication [68]. The study reveals that nelfinavir can strongly prevent the replication of SARS-CoV in Vero E6 cells [69]. So it can also be a good option in the treatment of COVID-19 patients.

3.9 Arbidol

Arbidol has been used in the treatment of influenza and other respiratory viral infections. Arbidol has been found to have an antiviral effect in early viral replication *in vitro* for SARS-CoV [70]. The study indicates that a combination of

arbidol with LPV/RTV can delay the progression of lung lesions and lower the possibility of respiratory and gastrointestinal transmission for decreasing the viral load of COVID-19 [71]. Therefore, arbidol can also be effective in COVID-19 cases.

3.10 Nitric Oxide

Nitric oxide (NO) is a short-lived, gaseous with biological activities. NO is originated from arginine by NO synthases. NO reacts with superoxide and produces peroxynitrite that can mediate bactericidal or cytotoxic reactions [72]. The research found that *in vitro* NO prevents the replication cycle of the severe acute respiratory syndrome coronavirus (SARS CoV) [73]. NO not only prevents the replication cycle of the severe acute respiratory syndrome but also inhibits viral protein and RNA synthesis. So nitric oxide can be an option to treat COVID-19 patients.

3.11 Doxycycline

Doxycycline is a second-generation tetracycline. It has broad-spectrum antimicrobial and anti-inflammatory activities [74,75]. A study has found that doxycycline combine with chloroquine prevents the entry of SARS-CoV-1 in cells [76]. So, doxycycline can also be effective in COVID-19 treatment.

3.12 Ivermectin

Ivermectin is a widely used drug for the treatment of several neglected tropical diseases and their control [77]. With over 2.5 billion doses delivered over the past 30 years, the drug has an excellent safety profile, and its potential to reduce malaria transmission by killing mosquitoes is under investigation in many trials around the world [78]. Ivermectin prevents the replication of certain positive, single-stranded RNA viruses *in vitro*, namely dengue virus (DENV), Zika virus, yellow fever virus, and others [79]. Clay et al. recently reported that ivermectin is a potent inhibitor of *in vitro* replication of the severe acute respiratory coronavirus 2 (SARS-CoV-2) [80]. Within 48h, the single treatment of this drug was able to reduce the virus in culture by up to 5000 times.

3.13 Favipiravir

Favipiravir is a drug developed for use against influenza and has been used successfully in other infectious conditions [81]. Favipiravir attacks the RNA viruses by inhibiting RNA dependent RNA polymerase [82]. It was the first

drug approved for coronavirus treatment in China. The use of Favipiravir as a treatment for coronavirus was approved by The National Medical Products Administration of China.

3.14 Plasma Therapy

It is no new idea to use convalescent plasma to treat viral diseases. It had already been tried at the beginning of the 20th century [83]. It was a time when there was no effective antiviral agent. Since then, several attempts have been made at convalescent plasma therapy [84]. Convalescent plasma or immunoglobulins is used as a last resort to increase the survival rate of SARS patients, whose condition continued to deteriorate following pulsed methylprednisolone therapy. In addition, some studies of patients treated with convalescent plasma showed a shorter hospital stay and lower mortality than those not treated with convalescent plasma [85]. In 2014, the use of convalescent plasma collected from patients who had recovered from the Ebola virus disease was recommended by WHO as an empirical treatment during outbreaks [85].

4. CONTROL

Immediate public health and infection control responses are necessary to limit the global spread of the virus and to diminish the damage associated with COVID-19 [86]. Travel history is more effective than chest radiography to detect and isolate SARS-CoV-2 pneumonia cases early which is known from experiences of an early phase of SARS-CoV-2 pneumonia [87]. WHO recommends some control measures to decrease the general risk of transmission of acute respiratory infections based on previous experience of MERS and SARS infections:

- Avoiding close contact with people suffering from acute respiratory infections
- Frequent hand-washing especially after direct contact with ill people or their environment
- Avoiding unprotected contact with farm or wild animals
- Suspected people with symptoms of ARI should practice cough etiquette maintaining distance, covering coughs, sneezing with disposable tissues or clothes, and washing hand
- Specialized and standard infection prevention and control practices should be

followed within health care facilities especially in emergency departments [88].

A study of MacIntyre & Wang has found that physical distance of 1 m in both health-care and community settings reduces the risk of 82% (adjusted odds ratio [aOR] 0.18, 95% CI 0.09–0.38) and each extra 1 m of distancing increases the relative protection more than doubled, with existing data up to 3 m (change in relative risk [RR] 2.02 per m; interaction=0.041). This study strongly holds up community physical distancing guidelines and proves that physical distancing is important to attain risk reduction. Moreover, this study also promotes societal restrictions and cautious ways of gathering in society [89]. According to the Chu and colleagues' masks and respirators decrease the risk of infection by 85% (aOR 0.15, 95% CI 0.07–0.34). They have also found that masks and respirators have more effective results in health-care settings (RR 0.30, 95% CI 0.22–0.41) than in the community (0.56, 0.40–0.79; pinteraction=0.049). They ascribe this difference to the most important use of N95 respirators in health-care settings. They had also found that respirators were 96% effective (aOR 0.04, 95% CI 0.004–0.30) where other masks were 77% effective (aOR 0.33, 95% CI 0.17–0.61; pinteraction=0.090) in a sub-analysis. As infection via the optical route might occur by aerosol transmission or self-inoculation in health care settings, Chu and colleagues found that eye protection resulted in a 78% reduction in infection (aOR 0.22, 95% CI 0.12–0.39); [90].

Respirators and multilayer masks are reported to be more protective than single layer masks by Chu and colleagues. A good quality cloth mask should be multi-layered with a good facial fit and the fabric should be water-resistant [91]. As masks were equally effective in both health-care and community settings when adjusted for type of mask use and growing evidence for pre-symptomatic and asymptomatic transmission of SARS-CoV-2 supports universal face mask and social distancing [91,92]. Using face masks (even modestly effective) along with physical distancing could reduce the risk of transmission (flatten the curve) In the Areas with a high caseload of COVID-19 [93]. The use of a Universal face mask could be an effective way to reduce restrictions in communities which is important for continuing normal activities of daily life and could keep people safe in crowded settings and even in households. A study by Wang showed that secondary transmission of SARS-Cov-2 was prevented in Beijing, China by

the use of masks within households worn before the onset of disease [94].

Lastly, all the recent studies showed that one protective measure alone is not enough and it is important to use combinations of different measures such as physical distancing, face mask use, frequent hand washing, isolation of affected cases, and other interventions to mitigate the COVID-19 pandemic. We must follow these measures until we have an effective vaccine.

5. CHALLENGES

Though the whole world's efforts to understand COVID-19, many issues remain unclear and they have to face new challenges every time. First, one report has demonstrated that the presence of SARS-CoV-2 inpatient stools [95]. However, whether SARS-CoV-2 can be transmitted through the fecal-oral route remains unclear. Second, previous studies showed that SARS-CoV and as well as other coronaviruses could survive on environmental surfaces and inanimate objects however, the presence of SARS-CoV-2 in the environment has not been reported [96,97]. Other studies have shown that coronaviruses could be effectively 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 di-gluconate were less effective [97]. However, the current investigation of the efficacy of commonly used disinfection agents against SARS- CoV-2 is lacking. Third, although in many countries travel restriction was exerted, whether this intervention was effective is unclear. Fourth, although one case responded well to remdesivir and one *in vitro* study showed that remdesivir and chloroquine were promising for the treatment of COVID-19, further more clinical trials on the effectiveness of remdesivir and chloroquine for treating SARS-CoV-2 pneumonia should be conducted [98]. Fifth, although several studies have reported the clinical features of COVID-19, all of the patients had pneumonia and were treated in Wuhan and Beijing [99-102]. Finally, although 32.4% ($n = 90$) of the reported 278 cases with SARS-CoV-2 pneumonia received systemic steroid therapy, a study on the temporal features of the SARS-CoV-2-induced inflammatory response in relation to the timing of therapeutic interventions is lacking [99-101].

Multiple challenges to research exist during pandemics. First, the surge of the disease often outpaces the traditional steps for research, including protocol design, securing of funding, and ethics approval, all amidst busy clinical work. Pre-approved adaptable plans drawn prior to an outbreak are useful. For example, several interventions against SARS-CoV-2 are being incorporated into the Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP), a pre-approved platform trial for severe community-acquired pneumonia. Second, many ongoing studies of COVID-19 are single-center and underpowered to detect significant differences in meaningful outcomes between arms [103].

6. CONCLUSION

In this article, we curtail all the potential interventions for COVID-19 infection according to previous treatments of SARS and MERS. We have found that to enhance host immune response against RNA viral infection the general treatments are very important. The immune response has often been shown to be weakened by inadequate nutrition in many model systems as well as in human studies. Present all countries in the world face challenges to control this pandemic besides it is hard to control for densely populated countries. Scientists or specialists should work with human nutrition to develop their immune system to fight against the SARS-CoV-2 virus and as well as the future pandemic.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGMENTS

The authors would like to acknowledge the support of all co-authors to prepare and submit the article.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not

intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Perrella A, et al. Editorial–Novel Coronavirus 2019 (Sars-CoV2): a global emergency that needs new approaches. *Eur Rev Med Pharmacol.* 2020;24:2162-2164.
2. Pourhossein B, Dabbagh A, M. Fazeli, Insights into the SARS-CoV2 Outbreak; the Great Global Challenge: A Mini Review. *Journal of Cellular & Molecular Anesthesia.* 2020;5(1):23-26.
3. Banerjee A, et al. Bats and coronaviruses. *Viruses,* 2019;11(1):41.
4. Schoeman D, Fielding BC, Coronavirus envelope protein: current knowledge. *Virology journal.* 2019;16(1): 69.
5. Zumla A, Hui DS, Perlman S, Middle East respiratory syndrome. *The Lancet.* 2015; 386(9997): 995-1007.
6. Li Q, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England Journal of Medicine;* 2020.
7. Chen Y, Liu Q, Guo D, Emerging coronaviruses: genome structure, replication, and pathogenesis. *Journal of medical virology.* 2020;92(4):418-423.
8. Zhang N, et al. Recent advances in the detection of respiratory virus infection in humans. *Journal of Medical Virology.* 2020;92(4): 408-417.
9. Chan JFW, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerging Microbes & Infections.* 2020; 9(1):221-236.
10. Brown KM, Arthur J, Selenium, selenoproteins and human health: A review. *Public Health Nutrition.* 2001; 4(2b):593-599.
11. Semba RD, Vitamin A and immunity to viral, bacterial and protozoan infections. *Proceedings of the Nutrition Society.* 1999; 58(3):719-727.

12. Villamor E, et al. Vitamin A supplements ameliorate the adverse effect of HIV-1, malaria, and diarrheal infections on child growth. *Pediatrics*. 2002;109(1):e6-e6.
13. Jee J, et al. Effects of dietary vitamin A content on antibody responses of feedlot calves inoculated intramuscularly with an inactivated bovine coronavirus vaccine. *American Journal of Veterinary Research*. 2013;74(10):1353-1362.
14. West CE, et al. Epithelia-damaging virus infections affect vitamin A status in chickens. *The Journal of Nutrition*. 1992; 122(2):333-339.
15. Trottier C, et al. Retinoids inhibit measles virus through a type I IFN-dependent bystander effect. *The FASEB Journal*. 2009;23(9):3203-3212.
16. Health, N.I.o. Vitamin A. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/VitaminA-HealthProfessional/#:~:text=The%20top%20of%20sources%20of,squash%20%5B4%2C5%5D>
17. Powers HJ, Riboflavin (vitamin B-2) and health. *The American Journal of Clinical Nutrition*. 2003;77(6):1352-1360.
18. Keil SD, Bowen R, Marschner S, Inactivation of Middle East respiratory syndrome coronavirus (MERS-CoV) in plasma products using a riboflavin-based and ultraviolet light-based photochemical treatment. *Transfusion*. 2016;56(12):2948-2952.
19. Kyme P, et al. C/EBP ϵ mediates nicotinamide-enhanced clearance of *Staphylococcus aureus* in mice. *The Journal of Clinical Investigation*. 2012; 122(9):3316-3329.
20. Jones HD, et al. Nicotinamide exacerbates hypoxemia in ventilator-induced lung injury independent of neutrophil infiltration. *PLoS One*. 2015;10(4).
21. Xchange.sg H. Vitamin B: Best food sources and signs of deficiency. Food Tips. Available:<https://www.healthxchange.sg/food-nutrition/food-tips/vitamin-b-best-food-sources-signs-deficiency>
22. Hemilä H, Vitamin C and SARS coronavirus. *Journal of Antimicrobial Chemotherapy*. 2003;52(6):1049-1050.
23. Atherton J, Kratzing C, Fisher A, The effect of ascorbic acid on infection of chick-embryo ciliated tracheal organ cultures by coronavirus. *Archives of Virology*. 1978; 56(3):195-199.
24. Field CJ, Johnson IR, Schley PD, Nutrients and their role in host resistance to infection. *Journal of Leukocyte Biology*. 2002;71(1):16-32.
25. Hemilä H, Vitamin C intake and susceptibility to pneumonia. *The Pediatric Infectious Disease Journal*. 1997;16(9): 836-837.
26. Health N.I.o. Vitamin C. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/>
27. Tangpricha V, et al. Vitamin D insufficiency among free-living healthy young adults. *The American Journal of Medicine*. 2002; 112(8):659-662.
28. Holick MF, Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *The American Journal of Clinical Nutrition*, 2004;80(6):1678S-1688S.
29. Nonnecke B, et al., Acute phase response elicited by experimental bovine diarrhea virus (BVDV) infection is associated with decreased vitamin D and E status of vitamin-replete peruminant calves. *Journal of Dairy Science*. 2014;97(9):5566-5579.
30. Health N.I.o. Vitamin D. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/>
31. Galmés S, Serra F, Palou A, Vitamin E metabolic effects and genetic variants: A challenge for precision nutrition in obesity and associated disturbances. *Nutrients*. 2018;10(12):1919.
32. Beck MA, et al. Vitamin E deficiency intensifies the myocardial injury of coxsackievirus B3 infection of mice. *The Journal of Nutrition*. 1994;124(3):345-358.
33. Beck MA, Increased virulence of coxsackievirus B3 in mice due to vitamin E or selenium deficiency. *The Journal of Nutrition*. 1997;127(5):966S-970S.
34. Health N.I.o. Vitamin E. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/VitaminE-HealthProfessional/>
35. Cai C, et al. Macrophage-derived extracellular vesicles induce long-lasting immunity against hepatitis C virus which is blunted by polyunsaturated fatty acids. *Frontiers in Immunology*. 2018;9:723.
36. Begin M, Manku M, Horrobin D, Plasma fatty acid levels in patients with acquired

- immune deficiency syndrome and in controls. Prostaglandins, leukotrienes and essential fatty acids. 1989;37(2):135-137.
37. Morita M, et al. The lipid mediator protectin D1 inhibits influenza virus replication and improves severe influenza. *Cell*. 2013; 153(1):112-125.
 38. Leu GZ, Lin TY, Hsu JT. Anti-HCV activities of selective polyunsaturated fatty acids. *Biochemical and Biophysical Research Communications*. 2004;318(1): 275-280.
 39. Health N.I.o. Omega-3 Fatty Acids. Dietary Supplement Fact Sheets; 2019. Available:<https://ods.od.nih.gov/factsheets/Omega3FattyAcids-HealthProfessional/>
 40. Guillin OM, et al. Selenium, selenoproteins and viral infection. *Nutrients*. 2019;11(9): 2101.
 41. Harthill M, Micronutrient selenium deficiency influences evolution of some viral infectious diseases. *Biological Trace Element Research*. 2011;143(3):1325-1336.
 42. Beck MA, et al. Rapid genomic evolution of a non-virulent coxsackievirus B3 in selenium-deficient mice results in selection of identical virulent isolates. *Nature Medicine*. 1995;1(5):433-436.
 43. Health N.I.o. Selenium. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/>
 44. Maares M, Haase H, Zinc and immunity: An essential interrelation. *Archives of Biochemistry and Biophysics*. 2016;611: 58-65.
 45. Tuerk MJ, Fazel N, Zinc deficiency. *Current Opinion in Gastroenterology*. 2009; 25(2):136-143.
 46. Awotiwon AA, et al. Zinc supplementation for the treatment of measles in children. *Cochrane Database of Systematic Reviews*. 2017;6.
 47. te Velthuis A, et al. Zn²⁺ Inhibits Coronavirus and Arterivirus RNA Polymerase Activity *In Vitro*; 2010.
 48. Health N.I.o. Zinc. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/>
 49. Wessling-Resnick M, Crossing the iron gate: why and how transferrin receptors mediate viral entry. *Annual Review of Nutrition*. 2018;38:431-458.
 50. Jayaweera JAAS, Reyes M, Joseph A, Childhood iron deficiency anemia leads to recurrent respiratory tract infections and gastroenteritis. *Scientific Reports*. 2019; 9(1):1-8.
 51. Health N.I.o. Iron. Dietary Supplement Fact Sheets; 2020. Available:<https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/>.
 52. Prabakaran P, et al. Potent human monoclonal antibodies against SARS CoV, Nipah and Hendra viruses. *Expert Opinion on Biological Therapy*. 2009;9(3):355-368.
 53. Savarino A, et al. Effects of chloroquine on viral infections: an old drug against today's diseases. *The Lancet Infectious Diseases*. 2003;3(11):722-727.
 54. Delvecchio R, et al. Chloroquine, an endocytosis blocking agent, inhibits Zika virus infection in different cell models. *Viruses*. 2016;8(12):322.
 55. Gautret P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *International Journal Of Antimicrobial Agents*. 2020:105949.
 56. Ho, TY, et al. Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction. *Antiviral Research*. 2007;74(2):92-101.
 57. Mind for better mental health. Antipsychotics A–Z; 2017. Available:<https://www.mind.org.uk/information-support/drugs-and-treatments/antipsychotics-a-z/promazine/>.
 58. Khodadadi E, et al. Study of combining virtual screening and antiviral treatments of the Sars-CoV-2 (Covid-19). *Microbial Pathogenesis*. 2020;104241.
 59. Cauwenberghs S, et al. Shedding of procoagulant microparticles from unstimulated platelets by integrin-mediated destabilization of actin cytoskeleton. *FEBS letters*. 2006;580(22):5313-5320.
 60. Takahashi S, et al. Nicotianamine is a novel angiotensin-converting enzyme 2 inhibitor in soybean. *Biomedical Research*. 2015;36(3):219-224.
 61. Graci JD, Cameron CE, Mechanisms of action of ribavirin against distinct viruses. *Reviews in Medical Virology*. 2006;16(1): 37-48.
 62. Ksiazek TG, et al. A novel coronavirus associated with severe acute respiratory syndrome. *New England Journal of Medicine*. 2003;348(20):1953-1966.
 63. Liu J, et al. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic

- coronaviruses SARS-CoV, MERS-CoV, and 2019-nCoV. *Journal of Medical Virology*. 2020;92(5):491-494.
64. Tan EL, et al. Inhibition of SARS coronavirus infection *in vitro* with clinically approved antiviral drugs. *Emerging Infectious Diseases*. 2004;10(4):581.
 65. Vickers NJ, Animal Communication: When I'm Calling You, Will You Answer Too? *Current Biology*. 2017;27(14): R713-R715.
 66. Grein J, et al. Compassionate use of remdesivir for patients with severe Covid-19. *New England Journal of Medicine*; 2020.
 67. Sheahan TP, et al, Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nature Communications*. 2020;11(1):1-14.
 68. Lewis II, JS, et al. Protease inhibitors: a therapeutic breakthrough for the treatment of patients with human immunodeficiency virus. *Clinical Therapeutics*. 1997;19(2): 187-214.
 69. Yamamoto N, et al. HIV protease inhibitor nelfinavir inhibits replication of SARS-associated coronavirus. *Biochemical and Biophysical Research Communications*. 2004;318(3):719-725.
 70. Khamitov R, et al. Antiviral activity of arbidol and its derivatives against the pathogen of severe acute respiratory syndrome in the cell cultures. *Voprosy Virusologii*. 2008;53(4):9-13.
 71. Deng L, et al. Arbidol combined with LPV/r versus LPV/r alone against Corona Virus Disease 2019: A retrospective cohort study. *Journal of Infection*; 2020.
 72. Robbins RA, MB Grisham. Nitric oxide. *The international Journal of Biochemistry & Cell Biology*. 1997;29(6):857-860.
 73. Åkerström S, et al. Nitric oxide inhibits the replication cycle of severe acute respiratory syndrome coronavirus. *Journal of Virology*. 2005;79(3):1966-1969.
 74. Michalopoulos AD, A clinical and laboratory study of doxycycline ('Vibramycin'): A broad-spectrum antibiotic. *Current Medical Research and Opinion*. 1973;1(8):445-455.
 75. Cazalis J, et al. Doxycycline reduces lipopolysaccharide-induced inflammatory mediator secretion in macrophage and ex vivo human whole blood models. *Journal of Periodontology*. 2008;79(9):1762-1768.
 76. Gendrot M, et al. *In vitro* antiviral activity of doxycycline against SARS-CoV-2.
 77. Ômura S, Crump A, Ivermectin: Panacea for resource-poor communities? *Trends in Parasitology*. 2014;30(9):445-455.
 78. Roadmappers I, A Roadmap for the Development of Ivermectin as a Complementary Malaria Vector Control Tool. *The American Journal of Tropical medicine and Hygiene*. 2020;102(2s):3-24.
 79. Chaccour C, et al. Ivermectin and Novel Coronavirus Disease (COVID-19): Keeping Rigor in Times of Urgency. *The American Journal of Tropical Medicine and Hygiene*; 2020.
 80. Caly L, et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*. *Antiviral Research*. 2020; 104787.
 81. Kramer DG, et al. Favipiravir as a potential drug in the treatment of COVID-19. *International Journal of Research-Granthaalayah*. 2020;8(4):7-12.
 82. Berger K. Everything we know about Favilavir, the potential coronavirus treatment; 2020. Available:<https://www.singlecare.com/blog/news/favilavir-for-coronavirus/>
 83. Mair-Jenkins J, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: A systematic review and exploratory meta-analysis. *The Journal of Infectious Diseases*. 2015;211(1):80-90.
 84. Yoo JH, Convalescent Plasma Therapy for Corona Virus Disease 2019: a Long Way to Go but Worth Trying. *Journal of Korean Medical Science*. 2020;35(14).
 85. Chen L, et al. Convalescent plasma as a potential therapy for COVID-19. *The Lancet Infectious Diseases*. 2020;20(4): 398-400.
 86. Song F, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology*. 2020;295(1):210-217.
 87. Lim J, et al. Case of the index patient who caused tertiary transmission of COVID-19 infection in Korea: the application of lopinavir/ritonavir for the treatment of COVID-19 infected pneumonia monitored by quantitative RT-PCR. *Journal of Korean Medical Science*. 2020;35(6).
 88. Lai CC, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. *International Journal of Antimicrobial Agents*. 2020;105924.

89. Kim PS, Reicin AS, Discontinuation of VIOXX. *The Lancet*. 2005;365(9453):23.
90. Lu Cw, Liu Xf, Jia Zf, 2019-nCoV transmission through the ocular surface must not be ignored. *Lancet* (London, England). 2020;395(10224):e39.
91. MacIntyre CR, Wang Q. Physical distancing, face masks, and eye protection for prevention of COVID-19. *The Lancet*; 2020.
92. He X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature medicine*. 2020;26(5):672-675.
93. Ngonghala CN, et al. Mathematical assessment of the impact of non-pharmaceutical interventions on curtailing the 2019 novel Coronavirus. *Mathematical Biosciences*. 2020;108364.
94. Wang Y, et al. Reduction of secondary transmission of SARS-CoV-2 in households by face mask use, disinfection and social distancing: A cohort study in Beijing, China. *BMJ Global Health*. 2020; 5(5):e002794.
95. Guan Wj, et al. Clinical characteristics of coronavirus disease 2019 in China. *New England Journal of Medicine*. 2020; 382(18):1708-1720.
96. Casanova LM, et al. Effects of Air Temperature and Relative Humidity on Coronavirus Survival on Surfaces. *Applied and Environmental Microbiology*. 2010; 76(9):2712.
97. Eponyms A, Email/Username: Password: Remember me.
98. Wang M, Cao R, Zhang L. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019 nCoV) *in vitro* [published online February 4, 2020]. *Cell Res*. doi. 10.
99. Chen L, Han Yang F, Zhang tJ; 2001.
100. Yang X, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*; 2020.
101. Bai Y, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *Jama*. 2020;323(14):1406.
102. Chang D, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. *Jama*. 2020;323(11):1092-1093.
103. Phua J, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *The Lancet Respiratory Medicine*; 2020.

© 2020 Khan et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/61490>*