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Original Article

A Comprehensive Review Article on Severe Acute Respiratory Syndrome and Role of Antioxidants in its Prevention and Treatment

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ABSTRACT

The emergence of novel coronaviruses, including the severe acute respiratory syndrome and the more recent COVID-19 pandemic caused by SARS-CoV-2, has captured global attention due to their dangerous nature and potential for international harm. This comprehensive review delves into the historical evolution, virology, and clinical intricacies of these viruses. Beginning with the origins of SARS and its subsequent transmission, the article navigates through the epidemiology, pathogenesis, and clinical features, unraveling the complex interplay between these factors. Pivotal rigging role of antioxidants, including vitamins A, C, D, and pivotal minerals such as zinc, copper, selenium, and magnesium, is meticulously examined in relation to their potential to bolster immune responses and counteract oxidative stress. This review highlights the crucial significance of these antioxidants in both the prevention and treatment of viral infections. From the intricate virological structure to the transmission dynamics and the clinical manifestations that span from mild to severe, this paper meticulously unpacks the multifaceted nature of coronaviruses. Emphasizing the importance of swift intervention and preventive strategies, the article also explores antiviral therapies, convalescent plasma treatment, and vaccination efforts as essential tools in managing and preventing the spread of these viruses. The review underscores the necessity for collaborative research endeavors to fully comprehend and effectively combat these viral threats, thereby safeguarding global health and ensuring a resilient response to future outbreaks.

Keywords: SARS, Epidemiology, COV, Nutrition, Antioxidants.

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BACKGROUND

From the last two centuries, an unknown corona virus (COVSARS), the severe acute respiratory syndrome is gaining scientific attention because of its dangerous nature and potential to harm the globe internationally. The first case of SARS was emerged in 2002 in Foshan China. One case of MERS was also emerged in Saudi Arab, but it was slightly different from the former one [1]. This review is focused on the history, epidemiology, pathogenesis, clinical features, and role of antioxidants in treatment/prevention of SARS.

History

China was the first country to identify SARS-COV and SARS-CoV-2. Before 2003 only two COVs were known to cause disease. In November 2019 unusual cases were started to appear in China where mostly health workers got infected [2]. The SARS COV spread to 29 regions and became a global pandemic. Chains of transmission from one human to another occurred in Canada, Singapore, China and Hanoi. This special type of virus was first detected from the Wuhan city of China on December 31, 2019. In Pakistan, it was first detected on February 26, 2020, and within few months it was disseminated in the whole world (Koenig 2020). Till now the deaths reported due to the Corona virus is more than six million. Increasing patients and death rate has produced fear and horror in the whole population of the world [3].

Virology

A novel group of 2b beta coronavirus was identified as being responsive of this infection. But the structure was not even nearly close to any previous strains of COVSARS genome consisting of methylated cap 5′ and poly adenylated tail 3′. In SARS, the multiplication rate in the gene structure was 0.80–2.38×10–3 nucleotide changings per site, and the unsimilar and similar alteration rates were said to be 1.16-3.30 × 10-3 and 1.67-4.67× 10-3 per site per year, which are same with other RNA viruses [4].

Spread

It was an idea that SARS might have spread from animal species in the markets to humans as high occurrence was found in asymptomatic wild animal's salesmen. After detecting a highly similar form in palm civets in Shenzhen, they were thought to be responsible for SARS COV to humans because 30% were found to be positive for the virus. Soon in 2020, it was found out that horseshoe bats were involved in carrying SARS COV. But it remained uncertain that an immediate host is involved in the transmission of virus. Within a few days it was revealed that the main route of spread is through having a close contact with the infected person either via respiratory droplets or other objects [5].

Pathogenesis

The various COVS of animal origin performed evolution and genetic matches, resulting in differentiated COVS that maybe more harmful and be more deadly to humans. The pathogenesis of SARS is complicated as many factors are involved in its clinical manifestations. It can affect multiple organs other than the respiratory tract [6].

Histology

Many reports of SARS showed that mostly there is alveoli damage. The G- protein of the SARS COV decreases the ACE-2 affect that cause to increase in the oxidative stress in many patients and disturbs the oxidation reduction balance. It has been proven that diarrhea was present in 70% of SARS cases making it an important symptom to diagnose the SARS COV infection. The symptoms mainly showed up on day 10 of the illness as a result of high nasopharynx viral load [7].

Transmission

There are three primary ways to transmit the virus, including close person-to-person contact, droplet transmission, and transmission by touch. Droplet spread occurs when an infected person sneezes or coughs. Virus containing droplets are forced up to 3 feet through the air and accumulate on the mucous membranes of the mouth, nose, or eyes of persons who are nearby. Studies showed that this infection is a lethal disease that is spreading two weeks after exposure [8]. The overcrowded hospitals, improper ventilation and use of jet nebulizer was the major vehicle for its transmission and spread. It was also found in urine, secretions and even in tears of some infected patients. PCR testing showed SARS COV infection in the air around, swabs, beds, television, remote control, nursing stations, medication, refrigerator etc in Toronto. This thing forced to take necessary respiratory protection safety hygienic measures [9]. Many nosocomial transmissions were also involved such as spread of SARS infectious particles not getting a proper exist, poor ventilation system, infectious returning via drainage system, overcrowded places made easy long range airborne transmission(>200m), through fecal/oral route and non-living objects on various surfaces.

Clinical manifestations

Different clinical manifestations were seen in patients from mild, in moderation, severe, rapidly progressive to death.

Incubation period

average incubation period= 4.6 days
most of illness occurred= in 10 days
average time from symptoms to hospital= 2 to 8 days
average time from symptoms to IMV=11 to 23.7 days [10]

Symptoms

Fever, nonproductive cough, myalgia, sputum production, arthralgia, diarrhea, headache, vomiting, sore throat, dizziness, dyspnea, and chills are the symptoms of this infectious disease. Study showed that 6.7% of SARS patients had acute renal impairment and 84.6% had presence of protein in urine. Blood related problems such as thrombocytopenia and lymphopenia were most commonly seen in SARS problems showed for SARS-CoV-2 including ARDS, anemia, cardiac problems and secondary infection [11].

Lab diagnosis

Lab diagnoses about SARS were performed using reverse transcriptase PCR, urine, stools specimen, IgG antibodies, quantitative real time serum RNA and lymphocyte count.

Radiologic features

Radiographic features were nonspecific. Only High-Resolution Computer Tomography (HRCT) could detect the small lesions early. ARDS and pneumonia mediastinum were seen in severely ill patients continuously over a period of 3 weeks [12].

Prognostic markers and outcomes

The poor prognostic markers that lead to critical illness and death are advanced age, viral loads, conditions such as diabetes mellitus and chronic hepatitis B, lab markers: high lactate dehydrogenase, high LDH levels, increase in neutrophil count low amount of CD4, CD8 [13].

Antiviral and other potential treatments

Ribavirin was widely suggested for the treatment of SARS COV infected patients, but it did not seem so helpful because of its low efficacy on the patients. Clinical proofs did not support the use of cortisone treatment for SARS-CoV-2 lung damage [14].

Therapy by convalescent plasma

Plasma was given by several health care employees who got infected and recovered from this infection. Study showed that this therapy increases the survival rate and discharge rate among patients as compared to those who did not receive plasma. Early administration of plasma seemed more effective [15].

Prevention

Vaccine

S-protein is the major component in the SARS viral structure, and it could have an immune effect with an adenoviral vaccine that would produce a strong effect in SARS COV infection and could be a protective vaccine against the infection [16].

After SARS, making of a vaccine seemed to be the best idea to stop future SARS-COV cases. Although, there were many hurdles in SARS vaccine development. Firstly, researchers did not have a complete knowledge of the pathogenic mechanism of SARS-COV. Secondly, animal models of SARS-COV infection could not brace human disease because of different pathogenesis. Thirdly, in order to test the efficiency, many people must be tested in areas where the virus is found. Once the SARS epidemic ended, human trials were difficult [17].

General preventive measures

Prevention of transmission was necessary in order to stop this spread. The primary mode of transmission was direct contact with the infected ones so it was necessary to put them in quarantine until the infection goes so that the spread may reduce [18]. Public education and awareness were also necessary in this regard. Slaughterhouses, markets with wild animals and rearing transport were completely banned by the government [19]. The sale of small wild animals was also banned. Quarantine is an old but very successful measure to fight a destructive epidemic, but quarantine rules can be tough to apply. Some of the rigorous preventions that were necessary are environmental hygiene and personal hygiene of health care workers should be maintained, contact finding, strict isolation of actively ill patients and quarantine of close contacts should be imposed early, training in the use of PPE protects the safety of employees, establishing clinics, setting up hospital wards and SARS hospitals reduced human-to-human transmission and education of the public on spreading diseases and what measures to take personally to stop spread [20].

Hospital infection control measures

Hospital originated transmission was the most important point of the SARS pandemic as in 1706. 0ut of 8096 patients of SARS were health workers. Health care workers and the public should be wearing masks and protective kits. Hand gloves, masks, eye protectors, and hygiene should be maintained. Separate medical ward should be assigned for the infected patients [21].

Management

SARS infected patients can recover easily if proper care and management is being done. There is no proper treatment plan that can be done. Early the diagnosis, early the management. Some of the ways for SARS COV management are as soon as possible, suspicious and positive patients should be segregated and treated in designated hospitals under secure conditions, suspect cases ought to stay together in one room, according to the WHO, people with minor symptoms who do not have chronic conditions (such kidney failure, immune insufficiency, lung or heart disease, or renal failure) can get therapy in isolation at home, supportive care includes bed rest, a healthy diet, regular checks of vital signs and oxygen levels, dehydration prevention, and electrolyte and acid-base balance maintenance and supplemental oxygen can be given if oxygen saturation is reduced [22].

Nutritional aid in SARS

Nutrition is an important key to health. More importantly, nutrition has a role in the management of both acute and long-term illnesses, particularly those for which there is no known cure. This may apply to the SARS COV pandemic too. Emerging proofs shows that it is associated with negative outcomes in older, compromised patients [23]. This may also suggest that poor nutritional intake worsens the problems. Nutritional intervention can be most suitable in the early phase as most patients move from cough to dyspnea too fast. Not much information has emerged about the role of nutrition in pre-ICU patients, but it clearly helps in boosting immunity that keeps the infection from mild to moderate. ESPN suggests that nutrition through mouth via pipes may be given to the mechanical ventilation patients [24].

Oxidative stress has a big role in SARS COV virus. When the atoms in cell become too reactive, they create an oxidative stress that imbalances the redox state in the body leads to low immunity and the body becomes more prone towards infections. It might be the reason that the body loses its immunity with increase in age and is more exposed towards infections. Antioxidants however help to increase the immunity of the body at any age by keeping the balance right. Antioxidant defense has been identified in numerous studies as a crucial factor in determining the severity of the infection [25, 26]. It has been demonstrated that viral infections reduce or block the action of antioxidant enzymes, resulting in a reduction in antioxidant capacity while the body is infected. So, it is necessary to keep your immune system strong already to avoid any worst situation [27]. Researchers believe that superoxide dismutase, a crucial antioxidant enzyme, may be the cause of why SARS-COV-2 infections in elderly people are more severe. Although its precise function is unclear, oxidative stress may serve as a secondary factor in an increase in the rate of multiplication. ACE-2 is an important factor. The spike of the virus reduces the ACE-2. That is another reason why immunity through antioxidants is necessary apart from the changing, oxidative stress is also known to decrease the surfactant level in the lungs causing more harm to them [26, 28]. Reduced antioxidant defenses in lung tissue during SARS-COV-2 infections may enhance surfactant failure and thus result in worse clinical outcomes. According to the aforementioned data, youngsters and young adults who have better antioxidant capacities than elderly people do so to their benefit. But this does not mean immune power cannot be increased in elders. SThe first line of defense in the prevention and treatment of SARS-COV-2 infections, particularly in the elderly or patients with other conditions, is antioxidant drugs due to the strong correlation between infection severity and host antioxidant capability. Many antioxidants such as Vitamin A, Vitamin C, Vitamin D, Selenium, Copper, Zinc, Magnesium etc. plays an important role in boosting immunity [29].

Vitamin A

Vitamin A functions as a barrier, deficiency can expose the skin lining or cell lining of different organ systems and immunity will be mismatched. Serum retinol decreases during an infection, the greater the infection, the greater the loss of the serum. In this regard vitamin A diet in moderate amounts would not be a harm to the body and also aid in coping with the infection [30]. The foods that are rich sources of vitamin A are winter squashes, cantaloupe, fish, pink grapefruit, dark leafy greens, sweet potatoes, lettuce, bell peppers, carrots, and broccoli. The daily intake for Vitamin A is 900 micro gram of retinol equivalents activity (RAEs) [31]. Some of the foods are given in Table 1.

Table 1. Vitamin rich foods [32]

Food	Per cup	Per 100 grams	Per 200 calories
Carrot	1329 mg	1329 mg	1329 mg
Tuna	1287 mg	1287 mg	1287 mg
Butternut squash	1144 mg	1144 mg	1144 mg
Spinach	943 mg	943 mg	943 mg

Vitamin D

A major public health issue is vitamin D deficiency. Vitamin D have an immunity changing role on the immune system, secretes antiviral peptides [33]. Different mechanisms are used by vitamin D to lower the risk of viral infection and mortality [34]. To reduce the risk of common cold, there are three pathways used by vitamin D physical barrier, cellular natural immunity, and adaptive immunity. Many reviews stated that vitamin D could reduce viral infections. It accomplishes this by preserving cellular immunity, gap junctions, and cell junctions [35]. Acute respiratory distress syndrome can be brought on by vitamin D insufficiency. People with such conditions are more prone to viral infections. Also, sunlight is also associated with low infections from virus. Therefore, it has been suggested that vitamin D supplementation is effective for treating acute respiratory tract infections. Additionally, some studies have shown that taking vitamin D daily or once a week can help you manage infections. The recommended dosage for a month is up to 250 micrograms, which effectively raises the blood levels of 25 O[34] by 75–125 mol/L. After a month, the dosage can be lowered to 100 micrograms per day to keep the levels of 25 (OH) D in the blood stable [36]. The foods that contain vitamin D are listed in Table 2.

Table 2. Vitamin D rich foods [2]

Food	Mcg	serving (dv)	IUS %
Cod Liver oil	34.0	1360	170
Trout	16.2	645	81
Salmon cooked	14.2	570	71
Mushrooms	9.2	366	46
Milk	2.9	120	15
Sardines	1.2	46	6
Soy	2.5	100	13
Cereal	2.0	80	10
Egg	1.1	44	06
Liver, beef	1.0	42	5
Tuna fish	1.0	40	5
Cheese	0.3	12	2
Mushrooms	0.1	04	1

Vitamin C

In many physiological situations, vitamin C is a crucial substance with antioxidant capabilities. Low vitamin amount in malnourished patients were treated with vitamin C. Patients with sepsis and shock responded well to treatment with a mixture of hydrocortisone, ascorbic acid, and thiamine (HAT therapy). Different studies showed that vitamin C high doses are effective in viral infections. It is well established that vitamin C both acts as a strong antioxidant and promotes oxidation [37, 38]. A large dose of vitamin C is found helpful in viral infections, especially SARS COV. Vitamin-C has well-known biological and therapeutic effects in the management of critical care. This is further bolstered by the fact that high dosages of vitamin C have effectively treated viral ARDS [38, 39]. High doses of Vitamin C given promptly help with the SARS illness. Additional research demonstrated the effectiveness of vitamin C in preventing COV infections. It is believed that Vitamin C administered intravenously works particularly well by preventing COV-related cytokine storms from occurring. Vitamin C foods include kale, broccoli, kiwifruit, snow peas, strawberries, papayas, bell peppers, tomatoes, guavas, and oranges [40]. Vitamin C's current recommended daily intake is 90mg. Some of the vitamin C rich foods are given in Table 3.

Table 3. Vitamin C rich foods [41]

Food	Per cup	Per 100 grams	Per 200 calories
Strawberries	98mg	59 mg	368 mg
Kale	23mg	83mg	99mg
Bell pepper	152 mg	128mg	982mg
Orange	96 mg	53 mg	226mg
Broccoli	81 mg	89 mg	525mg
Kiwi fruit	167 mg	93 mg	304 mg
Papaya	88mg	61mg	283mg
Guava	377 mg	228 mg	671 mg
Tomato	55mg	23mg	283mg

It is now clear that high doses of vitamin C have proved helpful in coping viral infections. It is advised to take separate dosages of vitamin C totaling at least 3,000 milligrams (or more) every day. Vitamin C boosts immunity and has direct antiviral effects on numerous infections. You can take it as ascorbic acid, which tastes sour like vinegar and comes in capsules or crystals that can be dissolved in liquids like juice or water. Another non-acidic form of it is sodium ascorbate. It must be taken to bowel tolerance in order to be most effective [42].

Copper

Copper is an essential trace element and useful antioxidant. It is crucial for keeping the human immune system functioning properly. It affects how macrophages, neutrophils, natural killer cells, and T helper cells operate. These cells have a role in the creation of certain antibodies, cell-mediated immunity, and the destruction of pathogenic microorganisms. Humans who are deficient in copper experience immunological responses, bone, and connective tissue abnormalities, and WBCS deficiencies. If infants have Cu deficiency by birth, they can be more exposed to several infections that are harmful [43, 44]. As deficiency of copper can cause various problems so does the excess, that is why the amounts should always be in moderation. There is a critical balance that is maintained between the cells and virus, any disturbance can cause worst effects on the body. It is the fact that Cu deficient humans are more susceptible to infections [45]. Cu2+ was demonstrated in a cell-based study to inhibit papain-like protease-2, a protein required for SARS-CoV-1 replication and the best illustration of how antioxidants can assist prevent viral infection. The best food sources of copper are shellfish, seeds, nuts, organ meats, cereals made with wheat bran, whole grain goods, and chocolate. The amount of copper in the food has a significant impact on how much of it is absorbed; bioavailability ranges from 75% of dietary copper when the diet only comprises 400 mcg to 11% when the diet contains 7.5 mg per day [46]. Copper is present in cashew nuts dry roasted, mature seeds millet, sunflower seed kernels, simmered chocolate, dark tofu, baking chocolate, unsweetened potatoes, cooked flesh and skin, liver, dry figs, mushrooms, beef, roasted turkey, giblets, chickpeas, cooked salmon, medium potato, cooked whole wheat pasta, avocado, boiled spinach, asparagus, cooked cereals. Hence, we conclude that Cu supplementation and diet can help in fighting COV infection especially in older people where Cu deficiency is possible [47].

Zinc

Zinc is a popular dietary supplement that is produced as a standalone product or in combination with other vitamins, minerals, and nutrients. Most zinc supplements are consumed orally and can be taken in the form of lozenges, tablets, capsules, syrup, or both. Some products are administered intravenously or intramuscularly. The daily recommended dietary allowance [9] for zinc is approximately 2 mg for infants up to 6 months of age, and it gradually rises to 11 mg for men and 8 mg for women older than 13 years. For children aged 1-3 years, the acceptable upper limit for zinc is thought to be 7 mg, rising to 25 mg for adults and females of any age who are pregnant or nursing [48].

Zinc has the ability to inhibit (ACE2) activity and the doubling of SARS-COV RNA polymerase. As a vital co-factor with numerous physiological activities, zinc may also alter the host's response to an infection. Lack of zinc increases the risk of illness and immune system disturbance by lowering antibody and cell-mediated immunity in the body. Zinc plays a significant part in immune system functioning, tissue repair, and wound healing, all of which can slow or halt the recovery from viral infection. It is still unknown how exactly zinc works to treat SARS. Oysters, beef chuck roast, beef patty, baked beans, ½ breakfast cereal fortified, 25% of the DV for zinc chicken, dark meat, pumpkin seeds, yogurt low fat, cashews, cooked chickpeas, cheese, Swiss oatmeal, peas green etc. are important part of diet that provide zinc.

Selenium

Selenium is an important antioxidant as it has been studied that selenium deficient host is more exposed to viral infections [49]. In China, "Se-poor" soils range from 0.004 to 00.48 mg Se/kg; nevertheless, biogeochemical parameters such as soil mineralogy, acidity, oxidation potential, and the presence of organic matter restrict Se bioavailability to crops regardless of soil concentration. Selenium proved to be helpful in controlling the oxidative stress of the body, increases immunity and saves from infection. Daily dietary allowance and source for selenium is given in Table 4 and Table 5 respectively.

Table 4. Daily dietary allowance for selenium [42]

Age	Male	Female
-12 months	20mcg	20mcg
1-3 years	20mcg	20mcg
4-8 years	30mcg	30mcg
9-13 years	40mcg	40mcg
14-18 years	55mcg	55mcg
19-50 years	55mcg	55mcg

Table 5. Food source of selenium [48]

Food	Mcg percent	Percent DV
Brazil nuts	544	989
Tuna	92	167
Sardines	45	82
Ham	42	76
Shrimp	40	73
Macaroni	37	67
Beef steak	33	60

Turkey	31	56
Beef liver	28	51
Chicken	22	40
Cottage cheese	20	36
Brown rice	19	35
Beef	18	33
Egg	15	27
Bread	13	24
Baked beans	13	24
Oats	13	24
Milk	8	24
Yogurt	8	15
Lentils	6	11
Spinach	5	9
Cashew nuts	3	5
Corn flakes	2	4

MAGNESIUM

Because food processing eliminates magnesium from food and contemporary agriculture frequently fails to provide enough magnesium in the soil, many people are magnesium deficient. It is a crucial nutrient that is required for numerous metabolic pathways. Magnesium deficiency cannot be properly identified by a blood test for magnesium. A long-term magnesium deficit can develop in the body and may require higher-than-normal doses for six months or a year to correct [44, 50]. Foods that are rich in magnesium and recommended dietary allowance for magnesium are given in Table 6 and Table 7 respectively.

Table 6. Foods rich in magnesium [35]

Food	Mg per serving	DV %
Almonds	80	19
Spinach	78	19
Cashews	74	18
Peanuts	63	15
Cereals	61	15
Soy milk	61	15
Black beans	60	14
Edmame	50	12
Peanut butter	49	12
Potato	43	10
Brown rice	42	10
Yogurt	42	10
Breakfast cereals	42	10
Oatmeals	36	9
Kidney beans	35	8
Banana	32	8
Salmon	26	6
Milk	24-27	6
Halibut	24	6
Raisins	23	5
Bread	23	5
Avacado	22	5
Chicken breast	22	5
Beaf	20	5
Broccoli	12	3
White rice	10	2

Table 7. Recommended dietary allowance for magnesium [51]

Age	Male	Female
Birth to 6 months	30 mg	30 mg
7-12 months	75mg	75mg
1-3 years	80 mg	80 mg
4-8 years	130 mg	130mg
9-13 years	240mg	240mg
14-18 years	410mg	360mg
19-30 years	400mg	310mg
31-50 years	420mg	320mg

CONCLUSIONS

In conclusion, the emergence and evolution of SARS-CoV into COVID-19 underscores the importance of understanding these viruses. Their complex virology varied clinical manifestations, and rapid spread demand swift response and preventive measures. Antiviral therapies, convalescent plasma, and vaccination offer hope for management and prevention. The potential of antioxidants like vitamins A, C, D, and minerals such as zinc, copper, selenium, and magnesium to enhance immunity and combat oxidative stress is promising. Further research and collaboration are vital to effectively address these challenges and protect global health.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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