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A Review on Covid-19 Management and the Role of L-ascorbic Acid in the Co-V Medication Regimen

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Abstract

Since we all know that 2019–2021 were the most pandemic situation all over the world. The global COVID-19 pandemic has prompted significant research into effective management strategies and therapeutic interventions. Each and every age group was susceptible to the Co-V virus since it was new for everyone and the immune system couldn't recognize it and was unable to make that many potential antibiotics that could protect the people from being fought from it. Many of the people died all over the world, and there is no drug for the treatment of the disease. The mortality rate is very high throughout the country. Among the various potential treatments, vitamin C (L-ascorbic acid) has gained attention due to its immunomodulatory properties and potential to reduce the severity of viral infections. Vitamin C is an essential component that cannot be produced in the human body, but it is good against a wide range of upper respiratory infections, reducing hyper-inflammatory reactions and urge heal in infected areas. There are many findings, that prove that vitamin C has antioxidant, anti-inflammatory, anticoagulant, and immunomodulatory properties. The pneumonia patients are associated with low ascorbic acid levels and high oxidative stress. Pneumonia patients who consume vitamin C experience fewer harsh symptoms, and they are not much longer sick as patients not consuming vitamin C. In China and the United States, it has shown excellent results when a large proportion of intravenous L-Ascorbic acid is used for the management of Co-V.

The role of L-ascorbic acid in the management of COVID-19 as supplemental therapy was examined in this review. The survey focused on its biological mechanisms, such as enhancing immune function, acting as an antioxidant, and modulating inflammatory responses, all of which may encourage mitigating the pathophysiological effects of the virus.

Keywords: COVID-19, L-Ascorbic Acid and its Role, Antiviral Effect, Antioxidant, Modulating Inflammatory Responses

Introduction

Co-V

SARS CoV-2 is the virus causing COVID-19 and has brought a pandemic across the entire globe. First identified at Wuhan City in December 2019, its presence has stretched healthcare delivery and the economics of respective countries since then. In the transmission through respiratory droplets, efforts to slow it down have been greatly affected by the nature of this virus and several new strains it is spreading. In developed countries, the rapid spread of COVID-19 hospitals and strained medical resources pushed the healthcare systems to their limits. The mutation of the virus has resulted in sometimes more virulent variants like Delta and Omicron, creating further challenges for containment and vaccination strategies. A moment in history was marked by medical professionals and scientists who had focused on the virus, developing treatments and vaccines, being approved for emergency use within a year. However, vaccines were developed, yet this continued to jeopardize the global health initiatives due to challenges in vaccine distribution, misinformation campaigns, and increased dread of vaccinations. Besides the potential physiological effects, the psychological and social impacts of COVID-19 are very destructive. The impact is also long-term, and most countries are dealing with the virus itself and the precautions made in place to avoid the spread of the virus. Long-term COVID has increasingly been a cause for concern for individuals and medical bodies due to

symptoms persisting long after the infection. Some of the signs include fever, cough, fatigue, and loss of taste or smell, in extreme cases cause respiratory diseases failure of organs and even cause death, in most such cases, people affected range from the old to anyone suffering from any other disorder.

Corona virus is one of the single-stranded, spherical or pleomorphic RNA encapsulated in club-shaped glycoprotein. Among the corona viruses, four subtypes are there; alpha, beta, gamma, and delta viruses there are many varieties in each subtype of Corona viruses [1]. This disease can easily spread among various human subjects, creating aggravations with its severity; vaccination-related mass immunization, thus diminishing its more hazardous implications as long as COVID-19 persists in existence. Even still, unless reduced severity becomes associated with possible later emergent and further evolution to any more mild manifestation and is, instead anticipated due to advance immunological and/or better preparative surveillance strategies against possible related disease presentation that would appear due to variation.

Spreading Mechanism

The people of any age can be affected. Mainly infection is spread by large droplets of symptomatic patients which is produced during coughing and sneezing, although it can also happen to asymptomatic individuals and before symptoms appear [1, 2]. Research has proven that there is no difference in the viral burden between infected and uninfected individuals, but thatthe nasal cavity has larger viral loads than the throat. Patients may remain contagious even after they have recovered clinically and for as long as their symptoms persist. The main age group which are prone to affected by disease were between 50-65 years and males because of high level of ACE-2 concentration in the body [2]. Typically, corona virus is propagated by air borne zoonotic droplets. The cellular damage at the infected site is the result of viral replication in ciliated epithelium. The findings of a 2019 study show that the entry of the Corona virus in humans is followed by an ACE 2 enzyme, the exo-peptidase membrane, in the receptor [1, 2].

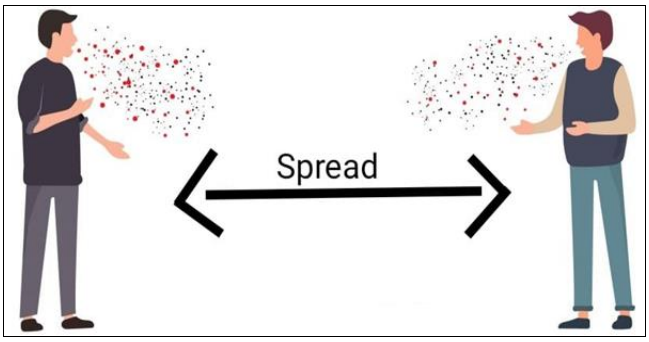

Fig 1: Mode of spreading Person to Person

Transmission process:-

Corona virus uses the spike protein-host cell protein interaction ANGIOTENSIN CONVERTING ENZYME-2 [ACE-2] in MERS-Co-V and DIPEPTIDYL PEPTIDASE-4 [DPP-4] in SARS-CoV to attach to the targeted cells [2, 4].The virus gene pool and capsid enclosed with viral nucleic acid are liberated into the host cell's cytoplasm and the receptor is recognized. The orf1A and orf1B genes found in the viral gene pool generate the two pp's, PP1a and PP1b, which aid to inhibit control of the host ribosomes for their self's translation process [4, 5]. The replication transcription complex is formed by both PP1a and PP1b. When pp is fabricated by protease 16'snspswere produced. Each nsps have different roles in the host body. One potential method of overcoming Corona virus infection is to induce destruction to the dimerization of nsp9. Every nspsplays a crucial part in replication along with transcription. M, E, and S are symphonized proteins entered into an ENDOPLASMIC RETICULUM-GOLGI INTERMEDIATE COMPARTMENT COMPLEX (ERGIC), which is then followed by the formation of a viral envelope [3].

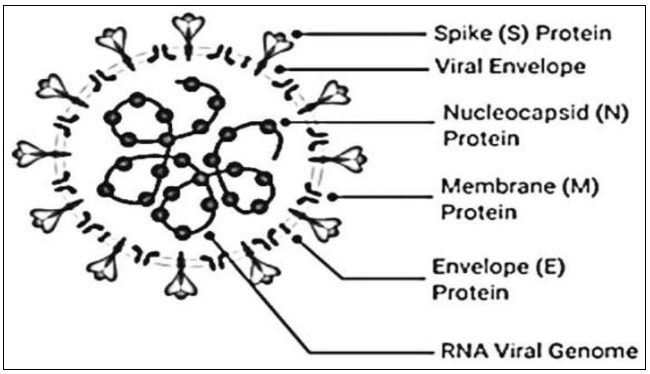

Fig 2: Anatomical structure of Corona Virus

Management:-

The COVID-19 management has intense care and management. Initially the Co-V susceptible patients are asymptomatic as the patient have a similar symptom as common cold and flu.

The identification to a covid positive patient is a bigger task for the health care professional. The patient without the viral infection should prevent themselves from the infectious patient. Infected patients having a symptom similar to that of a diseaseshould be isolated and then they are given with a high level of dose of different medicine regimen. Quarantine measure is mandatory to isolate infected patients, both symptomatic and asymptomatic, and person who may have been in contact with them [7].

The patient who are immunocompromised, pregnant, and are severely infected needs anurgent hospitalization. The variety of antimalarial, antiviral, antibacterial and glucocorticoid drugs are given for treating the infection [6], Anticoagulation therapy is also suggested for patients with the first half of COVID-19. Infection, inflammation, and other disease related variables can activate coagulation, raising the risk of intense ischemic events and disseminate intravascular coagulation [7].

The anti-malarial drugs, hydroxychloroquine and chloroquine, showed promising results in early *in vitro* study. And the patient kept in ventilator for providing a supportive care for respiration [6].

1) **Preventive care:**
   - Proper hand washing and the application of alcohol-based hand sanitation products [8].
   - Putting on masks within congested or dangerous environments.
   - Keeping a distance physically (6 feet/2 meters).
   - Avoid massive crowds and sealed-off areas that are prone to virus.
2) **Early recognition and separation:**
   - Keep track of signs, which include a high body

temperature, coughing, as well as difficulty in breathing [9].

- Early examination is essential for any individual who displays signs or has been at risk [9].
- Separation of confirmed infections to prevent spreading any further [10].

3) Vaccination:

- Complete immunizations as advised by medical authorities [11].
- Doses of boosters for populations at greater risk [12].

4) Therapy Procedures:

- Little symptoms require relaxation, hydration, as well as over-the-counter drugs [13].
- Conditions that vary from slight to deadly: People having a shortage of oxygen could do well with oxygen therapy [13].
- Use antiviral drugs (Remedesivir) as directed [13].
- In severe circumstances, corticosteroids can be given to manage swelling [13].

5) Public Safety Actions:

- Contact tracking and isolation for close interactions [14].
- Community instruction on prevention and signs [14].
- Ensuring sanitation in public places [14].

6) Recovery therapies:

- Involve physical exercises and breathing practices for pulmonary recovery as well [15].
- Examine for prolonged COVID symptoms such as tiredness or cognitive impairment [16].

7) Assistance with psychological health:

- It Involves psychological counselling and assistance organizations for dealing with anxiety and depression [17].
- Supporting psychological wellness by means of methods of relaxation and engaging in exercise.

8) Scientific study and investigation:

- Include tracking new variations along with treatments [18].
- Promote participating in clinical studies for COVID-19 breakthroughs [19].

9) Government support and Healthcare Strategy:

- Assure equal vaccine supply [20].
- Improving healthcare facilities for emergencies such as pandemics [21].
- Promoting global collaboration in dealing with outbreaks [22].

10) Supportive assistance:

- Health indicators and the level of oxygen will be closely observed [23].
- Conditions demanding prolonged therapy require inpatient treatment [24].
- A well-balanced diet along with good hydration is crucial for all living organisms [25].
- It has long been set that diet plays an important role in the treatment of viral infections, with crucial vitamins such as A, B1, B12, B6, C, and D, various essential and non-essential proteins, Alpha linoleic acid as well as minerals such as Fn, Zn, and Se [26].
- Vitamin C is one of the most common and widely used nutrients in nutritional support care playing a primary role.

Sodium Ascorbate (L-Ascorbic acid)

Despite significant advancements in understanding the pathophysiological mechanisms of COVID- 19, rephrasing this knowledge into effective remedial approaches remains a challenge. While vaccines have handed substantial benefits, they demand for new and effective treatments persists. Recent FDA- and EMA- approved innovative medicines show pledge in reducing mortality rates, but their high cost makes them less accessible, indeed bucolic nations. Since onset of the epidemicexperimenters have concentrated on motes with notable anti-inflammatory and antioxidant parcelsmaking interest in vitamin C unsurprising given its well- proved attributes [27]. Vitamin C are honoured as important antioxidantwith expansive literature describing extraordinary parcels.Its capability neutralize free revolutionaries has been linked to implicit benefits in conditions like cancer and coronary roadway complaint, which involve oxidative stress and towel damage. also, vitamin C's antioxidant goods sparked interest in its neuroprotective eventuality [27, 28]. Although some studies suggest a possiblepro-oxidative effect of vitamin C, clear *in vivo* substantiation remains fugitive, and threshold cure needed to spark similar goods is not well- defined. Vitamin C's influence on the vulnerable system is multifaceted [28]. When inordinate boluses might paradoxically suppress impunity, remedial boluses are known to enhance vulnerable responses. They include increased neutrophile exertionsimilar to chemotaxis and phagocytosisand enhanced T lymphocyte function and humoral responses. likewise, vitamin C plays pivotal part in connective towel health by sharing in collagen processes of conflations [29].

In the environment of COVID- 19 remedy, vitamin C's antiviral parcels particularly noteworthy. It inhibits viral replication, stimulates interferon product, and enhances antiviral exertion of lung epithelial cells.This broad Diapason conditioning punctuate its implicit clinical benefits. It's also essential to probe vitamin C insufficiency in cases with habitualnon-healing injuries, as this could have counteraccusations for their overall recovery [29, 30].

Fig 3: Possible effect of L-Ascorbic Acid

Antiviral effect of L-Ascorbic acid:-

L-Ascorbic Acid are explored for its potential antiviral effects, with some studies, including those by Linus Pauling, suggesting that high doses of vitamin C could be directly virucidal. This hypothesis was based on in-vitro findings, where elevated levels of vitamin C, in the presence of free copper or iron, generated hydrogen peroxide and reactive oxygen species with virucidal activity [31]. Additionally, the acidic pH of the experimental environment may have contributed to these effects. However, it is unlikely that such direct virucidal effects occur *in vivo*. While vitamin C is known as a potent antioxidant, it paradoxically exhibits pro-oxidant properties at high concentrations through the reduction of transition metals, generating reactive oxygen species. For instance, Avici demonstrated that high-dose

sodium ascorbate (90 mM) killed "Candida albicans" via iron-catalysed Fenton reaction, although this effect was nullified by the iron chelator 2,2′-bipyridyl [31, 32].

Despite limited direct virucidal activity *in vivo*, vitamin C has shown promise reducing viral loads through other mechanisms.Studie's have indicated that it may exert immunomodulatory effects, enhancing immune responses against infections. For example, Cinatl *et al* found that pre-treating human cells with vitamin C before cytomegalovirus (CMV) infection reduced viral antigen expression and viral load, an effect not observed when vitamin C was applied post-infection [32]. This suggests that vitamin C may modulate immune defence system rather than directly attacking viruses.Concentrated in leukocytes, lymphocytes, and macrophages, vitamin C enhances chemotaxis, neutrophile phagocytosis,oxidative, killingand lymphocyte proliferation and function.Animal studies, particularly those using Gulo (-/-) knockout mice, have provided valuable insights. These mice demonstrated increased susceptibility viral infections such as influenza, with higher lung viral loads, reduced interferon (IFN)-α/β production, and heightened inflammation compared to wild-type mice. Supplementation with vitamin C restored immune responses and reduced lung injury. Studies by Kim *et al* and Li *et al* showed that vitamin C improved immune function, reduced pro-inflammatory cytokines, and mitigated lung damage in these models. Moreover, Cai *et al* demonstrated that vitamin C reduced mortality and lung injury in restraint-stressed mice with H1N1 pneumonia, highlighting its role in restoring mitochondrial membrane potential and reducing pro-inflammatory gene expression [31]. Vitamin C has also shown activity against a variety of other viruses, including herpes viruses, poliovirus, rabies virus, and human immunodeficiency virus (HIV). Many viral infections trigger phagocyte activation and reactive oxygen species (ROS) release, contributing to both viral deactivation and host cell damage. In respiratory syncytial virus (RSV) infections, an oxidant-antioxidant imbalance plays a key role in pulmonary toxicity. Vitamin C, as a potent antioxidant, scavenges ROS and restores other antioxidants like tetrahydrobiopterin and α-tocopherol, potentially reducing oxidative damage and mitigating viral-induced injury [31, 32].

Immunomodulatory effect of vitamin C

Vitamin C, an essential micronutrient and antioxidant, plays a critical part in numerous redox responses. Discovered in the 1920s by Nobel laureate Albert Szent- Györgyi from Hungary, it was linked as vital for preventing scurvy.Beyond this, vitamin C exhibits notable immunomodulatory, antimicrobial, antiparasitic, antiviral, and antioxidant parcels [33]. Natural sources include citrus fruits, mangoes, strawberries, papayas, and tomatoes. As humans warrant L- gulono- γ- lactone oxidase, they can't synthesize vitamin C and bear salutary input. While 10 mg per day prevents scurvy, the recommended quotidian input for optimal health is 100 – 200mg [33, 34].

Vitamin C contributes to metabolism by supporting energy product, collagen emulsion and form, adrenal steroid and catecholamine product, and iron absorption. It serves as a vital cofactor in collagen emulsion, stabilizing its tertiary structure through responses interceded by prolyl and lysyl hydroxylase enzymes [33].

Vitamin C was demonstrated antimicrobial and antiviral parcels under colourful conditions. They inhibit the growth of "Pseudomonas aeruginosa" and "Staphylococcus aureus" *in vitro*, while also slightly reducing biofilm product in methicillin-resistant"Staphylococcus aureus"(MRSA)still, in pH-neutral surroundings,"Staphylococcus aureus" inhibition was not observed, although analogous conditions inhibited the growth of group A hemolytic streptococci in another study.Vitamin C showed weak inhibition of "Escherichia coli" ATCC 11775 growth but had stronger antiproliferative goods against "Escherichia coli" O157H7. In microaerobic conditions, 10 – 20 mg of vitamin C effectively inhibited "Helicobacter pylori" infection *in vitro*, when promoting its growth under aerobic conditions. These findings emphasize influence of attention, bacterial strainenvironmental factors of vitamin C's good inhibitory [33, 34].

In its oxidized form, L- dehydroascorbic acid(DHA),when vitamin C also displays antiviral parcels. DHA inhibits replication of herpes simplex contagion type 1(HSV- 1), rabies contagion, influenza contagion type A, and poliovirus type A. specially, the addition of Fe^{3+} the culture medium enhances DHA's antiviral exertion against HSV- 1 by generating hydroxyl free revolutionaries [34, 35].

Outcomes of L-Ascorbic acid in managing Co-V:-

Numerous investigations and studies proven that vitamin C has a very promising effect in reducing the symptoms of corona.

Vitamins administered intravenously should have a significant impact on reducing corona disease symptoms. The IV method is used to administer the large dose of ascorbic acid, and the potential outcome has been a decrease in CK cyclone [36]. Vitamin C is essential for avoiding viral infections, according to research performed in large population [37]. A severe lung problem is likely to arise in a patient with corona disease because of an increase in oxidative pressure and the production of free radicals. Vitamin C will most likely reverse these effects, which are most likely caused by this disease [37]. Ascorbic acid has demonstrated a strong anti-infection impact when there a low level of antioxidants in the body. Inflammation is caused by the body's inadequate levels of antioxidants and there will be reduced inflammation may result from ascorbic acid administrations and there will also a reduction of CK levels [38]. The investigations also demonstrated that there is an increase in body helper and killer T lymphocytes [38, 39]. These lymphocytes aid in boosting the host's immune system and ensuring that the body has enough antibodies to fight and recover from the illness.

Ascorbic acid dose 1gm\Day and Vitamin-E of 400 IU given to inpatient along with Hydroxychloroquine 400mg in Iran to study their combinational effect [40]. It was also studied that along with releasing oxidative stress and inflammation. Additionally, it has also been observing the reduction in secretion of Interleukin-6 induced by ET-1 from epithelial cells [40]. Ascorbic acid was later used by Americans as a nutritional medicine for preventing, treating, and managing COVID-19. In America, ascorbic acid is delivered through nasal inhalers as a method for a quick onset of action and systemic availability. They have demonstrated that a high blood level of ascorbic acid can reduce the viral burden and fortify the host body. There was a both direct and indirect activity shown in ascorbic acid.

Furthermore, giving ascorbic acid orally, intravenously, or through inhalation in combination with other medications regimen was widely accepted throughout the globe. Although their systemic availability and absorption vary but all of them have the same effect on the body. Both the oxidation of the viral envelope and the reduction of the viral capsid have antiviral properties that work in concert with other medications, making them a promising option for treatment (Quinacrine, Glycyrrhizin, Indian saffron, Xanthaurine) [41]. Development of pneumonia has been contributed in Covid-19 due to increasing in frequency of mucus secretion and since past L-ascorbic acid is utilized in treatment of pneumonia so this linkage furthermore enhances its concern for making its use in Covid-19 [42-43].

Conclusion

This article highlights the overall properties and role of L-ascorbic acid, which has a major impact on managing covid-19 symptoms and recovering from it. L-ascorbic acid, also known as sodium ascorbate and vitamin C, is majorly given in high dose via IV, Nasal, and, most promisingly, orally. The anti-oxidant, antiviral, and immunomodulatory properties of sodium ascorbate have a significant impact on getting relief as quickly as possible. The world know's how many people have suffered as a result of this epidemic, and while there is no drug to treat the pandemic, our TK plays an important role in the medication regimen. The Covid-19 treatment entails not only a drug regimen, but also strict adherence to the management approach. The strict routine checkup, nutrition, hygiene, and treatment should all be carried out concurrently to fight against the disease. The TK states that vitamins are an important element of our diet since they have virucidal, oxidative stress-releasing properties and work as an immunity booster for the body which mainly have the promising effect on treating viral infection. The combination of L-Ascorbic acid with various antiviral medicines (like Nirmatrelvir, Ritonavir, Molnupiravir) and antimalarial drugs (choroquine and quinoline) has a synergistic impact in the body. Aside from all of this, patients who have been exposed to covid and are likely to develop infection should quarantine themselves promptly for the sake of their neighbours.

The review has a pin point on a specific effect of L-ascorbic acid on reducing the number of covid patients which was firstly found to be useful treatment method in china and america, and it is now widely used worldwide for covid management and reduced the patient ventilatory support and therapy time. The Covid-19 is found to be a highly communicable disease worldwide and respiratory tract of the living organisms are the primary organ affected in this disease. Additionally, more reasearch were needed to gain better perception on how oral and IV Vitamin-C have affected on Covid-19 and Acute respiratory diseases.

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Conflict of Interest

The authors declare that no conflict of interest of any financial or other issues.

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