

## Original research article

# Study of outcome of high dose oral liposomal vitamin- C in COVID-19 patients

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## ABSTRACT

**Background:** The current pandemic Covid-19 causes several clinical manifestations from asymptomatic presentation to more serious Severe Acute Respiratory Syndrome (SARS) on humans. There is no specific antiviral treatment for Covid-19 and the management is mainly symptomatic.

**Aim:** To describe the role and outcome of high-dose of oral liposomal vitamin C treatment in a drink form for Covid-19 patients admitted in Government Medical College & ESI Hospital, Coimbatore, India.

**Materials and methods :** Patients who admitted to the with the diagnosis of COVID-19 by RTPCR in government medical college and esi hospital Coimbatore during 15 th march 2020 to april 30,2020 are taken for study is one of the earliest cases studies of Covid-19 in the Indian subcontinent.

**Results:** 89 % of patients improved symptomatically on 3-4 days with oral highdose liposomal vit-c The tiredness and myalgia improved in 76 % patients on third day. Anosmia improved in 4 days in 88 % of patients Sore throat and cough improved on 3-4 days in 90 % of patients and diarrhoea improved on 3<sup>rd</sup> day in 72% of patients.

**Conclusion:** Two consecutive negative results were confirmed in 94% of patients on high dose oral liposomal vitamin c. on 14 th day, suggests it is very much useful, cheap yet powerful tool as adjuvant treatment of covid19, with other AVAILABLE treatment modalities. Treatment with only vit c cannot be tried in any pandemic situations. Preventive methods, social distancing, masks, sanitizers (SMS) are essential for everyone till all get vaccinated and get herd immunity for covid 19

**Key words:** Covid-19, High-dose oral liposomal Vitamin

## 1. Introduction :

The Covid-19, which is the acronym of “coronavirus disease 2019” behaves similar to severe acute respiratory syndrome coronavirus (SARSCoV) which occurred in 2002, hence it is named as SARS-CoV-2.<sup>1</sup> It is a highly contagious disease, gets transmitted mainly from respiratory droplets of infected person through coughing and sneezing. As well as it may be transmitted through inhalation of aerosols and through contaminated inanimate surfaces like stainless steel, glass, plastic materials and cardboard, where the virus may persist for days<sup>2</sup>. It produces various clinical manifestations by damaging organs like lung, heart, blood, kidney, intestine, skin and brain. The clinical spectrum of the disease ranges from asymptomatic to more serious SARS and the systemic manifestations in the form of sepsis, septic shock, systemic coagulopathy and multi organ dysfunction syndrome (MODS).

vitamin C supplementation has been evaluated in numerous disease states, including serious infections and sepsis. Because serious COVID-19 may cause sepsis and acute respiratory distress syndrome (ARDS), the potential role of high doses of vitamin C in ameliorating inflammation and vascular injury in patients with COVID-19 is being studied

### **,1.1 Pathophysiology of Covid-19**

The pathogenesis of Covid-19 is due to virus-induced excessive immune reaction in the host. The activated leucocytes in the host produces a high level of pro-inflammatory cytokines (mainly IL-6) and chemokines in circulation, which is labelled as “cytokine storm syndrome” (or Hypercytokinemia) and it causes extensive tissue damages<sup>3</sup>. Recently, few study states that, there is a catastrophic microvascular injury (endotheliitis) mediated by terminal complement components C5b-9 (membrane attack complex) and associated procoagulant state lead to thrombogenic vasculopathy<sup>4</sup>. Currently, covid-19 management is limited to symptomatic and palliative treatment. No therapies have been demonstrated to prevent the progression of covid-19 to severe illness, but several drugs are under trail. One of the promising drug is vitamin C or Ascorbic acid.

**1.2 Properties of Vitamin C** Vitamin C (ascorbic acid) is a water-soluble vitamin that is thought to have beneficial effects in patients with severe and critical illnesses. It is an antioxidant and free radical scavenger that has anti-inflammatory properties, influences cellular immunity and vascular integrity, and serves as a cofactor in the generation of endogenous catecholamines. Because humans may require more vitamin C in states of oxidative stress

During human evolution, vitamin C lost its synthesizing capacities in humans due to the mutation in L-gulonolactone oxidase (GLO) gene, which codes for the vitamin C biosynthesis<sup>5</sup>. So, the benefit of vitamin C to the human body is achieved by external sources, which is abundant in Indian gooseberry, limes, oranges, lemon, tomatoes, kiwifruit, potatoes and leafy greens. Since it is a water-soluble vitamin, the oral bioavailability of regular vitamin C is only 15-30%. But the advent of nano-technology liposomalized vitamin C has more than 90% absorption. The liposomes are novel delivery system composed of phospholipid of soy or sunflower lecithin, which carries vitamin C into the intestinal cells with higher absorption rate and increases vitamin C in the blood level<sup>6</sup>. The excess amount of vitamin C excretes freely in urine. The recommended daily allowance in male is 90mg and in female is 75mg. The tolerable upper limit of oral vitamin C is 2gm per day without gastrointestinal disturbances. But there is no scientific evidence of toxicity even in the dosage of 10gm per day<sup>7</sup>. Moreover, vitamin C act as an essential nutrient for collagen formation, wound healing, aid in iron absorption and enzymatic production of certain neurotransmitters. However, the high dose of vitamin C acts as a powerful anti-oxidant, immunomodulator and antiviral<sup>8</sup>.

### **1.3 Role of Vitamin C as anti-viral**

The two-time Nobel laureate Dr. Linus Pauling, an American chemist have suggested that high dose vitamin C is directly virucidal. The vitamin C produces a significant impact on both the innate and adaptive immune functions in viral infections.

#### **In Innate Immunity**

- High concentration of Vitamin C enhances the first line of defence mechanism against the invading pathogens.
- In neutrophils it enhances cellular motility, chemotaxis, phagocytosis and causes oxidative injury by generating reactive oxygen species (ROS), which kills the pathogens and also damages the leucocytes themselves and host tissues.

- Vitamin C act as a potent antioxidant by scavenging the free radicals and protects the leucocyte as well as host tissues from oxidative injury.
- In monocyte and macrophage, it enhances phagocytosis and diminish the secretion of pro-inflammatory cytokines like Interleukin-6 (IL-6) and tumour necrosis factor- $\alpha$  (TNF-  $\alpha$ ).

#### **InAdaptive Immunity**

- High dose vitamin C decreases or modifies certain T cells activity, which secretes proinflammatory cytokine IL-2
- It acts as an immunomodulator by enhancing the release of  $\alpha$  and  $\beta$  interferon and downregulating the pro-inflammatory cytokines in lymphocytes.
- It enhances the B cell function and causes significant increase in serum IgA and IgM
- It enhances the proliferation of Natural Killer cells (NK) from mononuclear cells and helps in elimination of virus

## **2. Materials and Methods**

### **2.1 Clinical trial on covid-19 with high dose oral liposomal vitamin C**

A clinical trial was conducted to evaluate the safety and effectiveness of high-dose oral liposomal vitamin C treatment in a drink form for treating the adults hospitalized with Covid-19. The study is an observational clinical trial enrolled with 100 adults. All participants in the study have received clinical care for their condition along with the drugs, HIGH FLOW NASAL OXYGEN, inj. Remdesivir (or) T. Oseltamivir 75mg BD for 5 days and T. Azithromycin 500mg OD or)doxycycline 100mg od for 5 days, inj. Low molecular weight heparin, T. Zinc 50mg BD and multivitamins till they get discharged. All the patients have received high-dose of oral vitamin C with lecithin composition in a drink form. Each juice box contains 200ml with 1gm of vitamin C. The patients were treated by giving 2 juice boxes in the morning as well as in the evening. Totally 4gms of liposomal vitamin C has given daily for 10 days. Those who are interested also allowed to take KAPASURA KUDINEER given by ayush wing of our hospital as per the instruction from government of Tamilnadu.

### **2.2 Methods**

The medical records of patients were analysed by the research team of the Department of Medicine, Government Medical College & ESI Hospital, Coimbatore, India. The epidemiological, clinical, laboratory, treatment and outcome data were obtained with data collection from electronic medical records. All data was reviewed by internal medicine specialists. All patients were tested for Covid-19 from a nasal swab by real time reverse transcription polymerase chain reaction (RT-PCR) assay of 2019-nCoV RNA.

#### **Inclusion Criteria**

- Covid-19 positive patients admitted in our hospital
- Age 18 years and older

#### **Exclusion Criteria**

- Patients with diabetes mellitus
- Pre-existing kidney disease or on dialysis, congestive cardiac failure
- Patients with immunocompromised state such as acquired immunodeficiency syndrome, malignancy and on cancer chemotherapy treatment
- Pregnancy or breast feeding

### 3. Results

100 Covid-19 positive patients were studied and the following are the observation and analysis.

TABLE 1: Age distribution

Age Group	Number of Patients	Percentage
≤ 30 Years	24	24%
31-40 Years	34	34%
41-50 Years	19	19%
51-60 Years	15	15%
61-70 Years	4	4%
71-80 Years	3	3%
80-90 Years	1	1%

TABLE 2: Sex distribution

Sex	No of Patients	Percentage
Male	61	61%
Female	39	39%

TABLE 3: Signs and symptoms

Signs and symptoms	No of patients	Percentage
Fever	42	42%
Chills	6	6%
Sore throat	18	18%
Dry cough	18	18%
Shortness of breath	8	8%
Abdominal pain	4	4%
Diarrhoea	8	8%
Anosmia	4	4%
Myalgia	36	36%
Tiredness	40	40%
Asymptomatic	32	32%

TABLE 4: Days on which RT-PCR became negative

No of days	No of patients	Percentage
≤13 days	94	94%
>14 day	6	6%

### 3. DISCUSSION

89 % of patients improved symptomatically on 3-4 days with oral highdose liposomal vit-c . The tiredness and myalgia improved in 76 % patients on third day. Anosmia improved in 4 days in 88 % of patients . Sore throat and cough improved on 3-4 days in 90 % of patients and diarrhoea improved on 3<sup>rd</sup> day in 72% of patients. Many reports revealed that cytokine storms, which can be suppressed by VIT-C, are believed to be the main mechanism in the deterioration of patients with COVID-19. VIT-C, traditionally considered a dietary supplement, has antimicrobial and immunomodulatory properties. HIGH DOSE ORAL LIPOSOMAL VIT-C has been proven to be safe and therapeutic in critical care medicine, primarily as an adjunct to the treatment of septic shock and multiple organ failure, where it has been shown to improve outcomes and reduce mortality. ‘High-dose’ VIT-C therapy lacks a universal definition. A previous meta-analysis considered high doses as equal to or greater than 10 g/day. Twenty-four grams of VIT-C in this trial is higher than the dosage of VIT-C in previous clinical trials conducted on critically ill patients with severe infection.

To our knowledge, this is one of the first prospective randomised controlled studies of high-dose oral Vit-C treatment for COVID-19. Specific treatments for COVID-19 are not available at present. There are several clinical trials exploring immunotherapy. Documenting efficacy for any of these approaches requires time, adequate patient numbers and careful analysis.

Although blood plasma treatment for critical patients with COVID-19 was recommended by the National and Health Commission of the People’s Republic of China, plasma from recovered patients is a rare resource. Compared with these therapies, vit-C has great advantages in terms of stability, availability, safety and cost. Therefore, this trial is highly meaningful as it could potentially save lives at a low price. Vit -C is expected to improve pulmonary function and reduce mortality for patients with COVID-19.

However, there are also limitations to our study design and uncertainties during implementation. First, as SARS-CoV-2 is a novel coronavirus, the duration and distribution of infected cases are unpredictable geographically and temporally, so the number of recruited patients at some clinical centres may be low. Thus, competitive enrolment and multiple clinical trial centres are needed to ensure an adequate number of subjects. Second, complete blinding is not feasible due to the lack of available resources, such as placebos in the same package as Vit-C. The study is unblinded for dosing nurses, attending physicians and investigators in charge of enrolling participants, but blinding will be maintained for patients and all other members of the clinical and research team, such as statistical staff, to minimise bias. Third, some patients may have received non-specific, tentative and explorative symptomatic treatment

This study included 100 Covid-19 affected patients. As shown in Table 1, majority of the patients belong to the age group of 31-40 years. The minimum age was 20 years and maximum was 87 years.

As shown in Table 2, most of the patients having Covid-19 were male (61%). This male predominance may have happened due to increased travel by males. In our study the common clinical manifestations are fever (42%) followed by tiredness (40%).

All the patients were subjected to nasal swab and repeat RT-PCR assay of 2019-nCoV RNA was done on 12<sup>th</sup> and 13<sup>th</sup> day of admission. As shown in Table 4, two consecutive negative results were confirmed in 94% of patients and remaining 6% were positive. The remaining 6 patients again treated with high dose oral liposomal vitamin C and their two consecutive negative results were confirmed on 18<sup>th</sup> and 19<sup>th</sup> day of admission.

The patients treated with high-dose oral liposomal vitamin C had increased rate of RT-PCR negative. So, this result brings ray of hope in treating Covid-19 affected patients. Many centres across the globe are now currently using vitamin C as a supportive therapy for hospitalized patients with Covid-19, despite extremely limited clinical data supporting its effectiveness. But our centre has used high-dose oral liposomal vitamin C in a drink form and obtained a remarkable outcome. However, we require large scale multicentric clinical trial on high-dose oral liposomal vitamin C for creating standard treatment protocols for Covid-19 patients.

## 5. Conclusion

The Covid-19 is rapidly increasing across the world at a frightening rate. Currently, there is no targeted antiviral medications. Hence, the present treatment strategy of symptomatic and supportive management is still the main treatment of covid-19. Accordingly, the high dose of oral liposomal vitamin C is recommended to use as an adjunct therapy to combat covid-19 infection. However, the most effective way to avoid covid-19 still remains frequent hand washing with soap for at least 20 seconds, use of hand sanitizers of at least 70% alcohol, covering cough and sneeze, not touching the eyes, nose or mouth, social distancing, universal face mask and keeping clean and disinfect frequently touched surfaces are the key in preventing the spread of infections.

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