

# COVID-19: Up to 87% Critically Ill Patients Had Low Vitamin C Values.

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## Short report

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# Abstract

There are limited proven therapeutic options for the prevention and treatment of COVID-19. We underwent an observational study with the aim of measure plasma vitamin C levels in a population of adult ICU patients COVID-19 who met ARDS criteria according to the Berlin definition. This epidemiological study brings to light that up to 87% had low Vitamin C values. This observational study has the limitation it was undergone in a single center study. However, it shows an important issue. Given the potential role of vitamin C in sepsis and ARDS, there is gathering interest of whether supplementation could be beneficial in COVID-19. But, first of all, we had to know the incidence of vitamin C deficiency.

## Main Text

There are limited proven therapeutic options for the prevention and treatment of COVID-19. Given the potential role of vitamin C in sepsis and ARDS, there is gathering interest of whether supplementation could be beneficial in COVID-19 [1,2]. However, first of all, we have to know if the incidence of vitamin C deficiency is high.

We underwent an observational study with the aim of measure plasma vitamin C levels in a population of adult ICU patients COVID-19 who met ARDS criteria according to the Berlin definition [3]. Vitamin C levels were measured within the first 24 hours of ICU admission. The admission took place in ICU since first moment of hospitalization. The study was approved by the local Clinical Research Ethics Committee (PI-20-253).

We included 54 patients from Mars to April. Once the blood sample was drawn, it was quickly protected from light and processed with maximum speed. Vitamin C was determined by high-performance liquid chromatography (HPLC). The range of normality of vitamin C plasma values are 0.4-2 mg/dL. Up to 87% had low Vitamin C values. The median value of vitamin C was 0.13 mg/dL with a minimum value of <0.10 mg/dL and a maximum of 1.08 mg/dL; the mean value was 0.195 mg/dL and standard deviation was 0.181 mg/dL. There were 11 patients with a value of <0.10 mg/dL.

Main characteristics of the population included are presented in Table 1.

This observational study has the limitation it was undergone in a single center with small sample size of critically ill patients. However, it shows an important issue. Up to 87% critically ill COVID-19 patients have low Vitamin C values.

Vitamin C is an essential water-soluble nutrient, required as a cofactor for a number of enzymatic reactions [4]. Its effects on the immune system during infection include the promotion of phagocytosis and chemotaxis of leucocytes and development and maturation of T-lymphocytes.

Animal studies support a beneficial role of vitamin C. These positive effects include increased resistance of chick embryo tracheal organ cultures to infection and protecting broiler chicks against avian

coronavirus [5,6]. Vitamin C had been shown to significantly decrease serum TNF $\alpha$  and IL-1 $\beta$  levels and increased superoxide dismutase, catalase, and glutathione levels in a rat ARDS model supporting its antioxidant effect [7]. Additionally, vitamin C also enhances lung epithelial barrier function by promoting epigenetic and transcriptional expression of protein channels at the alveolar capillary membrane that regulate alveolar fluid clearance, which include aquaporin-5, cystic fibrosis transmembrane conductance regulator, epithelial sodium channel, and the Na<sup>+</sup>/K<sup>+</sup>-ATPase pump [8].

Research is ongoing with COVID-19 disease with a high-dose intravenous vitamin C (HDIVC) cohort study in progress in Palermo, Italy [9]. Recruitment has also begun on a new clinical trial investigating vitamin C infusion for severe 2019-nCoV-infected pneumonia in Wuhan, China. This is the first RCT to test whether there is a benefit of HDIVC in COVID-19. One-hundred and forty patients are planned to be treated with a placebo or HDIVC at a dose of 24 g/day for 7 days [10].

## List Of Abbreviations

SARS-CoV-2: name of this novel coronavirus, COVID-19: disease caused by SARS-CoV-2, ARDS: Acute Respiratory Distress Syndrome, ICU: Intensive Care Unit, SOFA: sequential organ failure assessment, ECMO: extracorporeal membrane oxygenation, AKI: acute kidney injury, CRRT: continuous renal replacement therapy, IRR: intermittent renal replacement, CKD: chronic kidney disease, ICU-LOS: Length of ICU stay, HOSP-LOS Length of hospital stay.

## Declarations

### Ethical Approval and Consent to participate

Clinical Research Ethical Committee approved the study

The Center's Clinical Research Ethics Committee considered there was no need to request informed consent

### Consent for publication

Not Applicable

### Availability of supporting data

Not Applicable

### Competing Interests

The authors declare no competing interests.

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### **Author's contributions**

The author(s) read and approved the final manuscript.

Lara Bielsa-Berrocal, MD. Contribution: This author collected the data and prepared the manuscript. This author helped design the study and prepared the manuscript. This author helped design the study and analysed the data.

This manuscript was handled by: Teresa M. Tomasa-Irriguible, Ph.D, M.D.

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## Tables

**Table 1.** Clinical characteristics of the COVID-19 patients included. Results of continuous variables are expressed as median and minimum and maximum. Categorical variables are expressed as frequency (percentage). SOFA sequential organ failure assessment, ICU intensive care unit, ECMO extracorporeal membrane oxygenation, AKI acute kidney injury, CRRT continuous renal replacement therapy, IRR intermittent renal replacement, CKD chronic kidney disease, ICU-LOS Length of ICU stay, HOSP-LOS Length of hospital stay.

<b>Clinical characteristics</b>	<b>COVID-19 with ARDS (n=54)</b>
Age (median, min-max, years)	60 (31 – 76)
Male (n, %)	41 (74.5)
SOFA score (median, min-max, points)	9 (2 – 17)
Intubation (n, %)	49 (89.1)
Prone position (n, %)	40 (72.7)
VV-ECMO (n, %)	3 (5.45)
VA-ECMO	1 (1.8)
Noradrenaline	40 (72.7)
Dobutamine	6 (10.9)
CKD	6 (10.9)
AKI	22 (40)
CRRT	3 (5.45)
IRR	2 (3.64)
Bacterial superinfection	23 (41.8)
ICU-LOS (median, min-max, days)	12 (1 -90)
HOSP-LOS (median, min-max, days)	25 (1 – 101)
Mortality (n, %)	15 (27.8)