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Up to 40% of COVID-19 Critically Ill Patients have Vitamin D Deficiency

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Abstract

Background: Coronavirus disease (COVID-19) has caused more than 745,000 deaths worldwide. Vitamin D has been identified as a potential strategy to prevent or treat this disease. The purpose of the study was to measure vitamin D at hospital admission of COVID-19; **Methods:** We included critically ill adult patients with a positive test for COVID-19 (with the polymerase chain reaction positive test for SARS-CoV-2), from March to April, 2020. Statistical significance was defined as $P < .05$. All tests were 2-tailed; **Results:** A total of 35 patients (median age, 60 years; 26 [74.3%] male) were included. Vitamin D levels were categorized as deficient for 14 participants (40%). Vitamin D deficiency was associated with lower levels of vitamin A (P= 0.003) and Zinc (P= 0.019) and also lower levels of albumin (P= 0.026) and prealbumin (P= 0.009). Overall, none of the studied variables were associated with vitamin D status: mortality, intensive care unit (ICU) or hospital stay, necessity of vasoactive agents, intubation, prone position, C reactive protein (CRP), Dimer-D, Interleukin 6 levels (IL-6), ferritin levels, or bacterial superinfection. **Conclusion:** In this single-center, retrospective cohort study, deficient vitamin D status was found in 40% in COVID-19 critically ill adult patients with Acute Respiratory Distress Syndrome (ARDS). However, deficient vitamin D status was not associated with inflammation or outcome.

Keywords: SARS-CoV-2, Covid-19, Vitamins.

Abbreviations

SOFA: sequential organ failure assessment; ICU: intensive care unit; ECMO: extracorporeal membrane oxygenation; CKD: chronic kidney disease; AKI: acute kidney injury; CRRT: continuous renal replacement therapy; IRR intermittent renal replacement; DVT: deep venous thrombosis; PE: pulmonary embolism; ICU-LOS: Length of ICU stay; HOSP-LOS: Length of hospital stay; Vit. D: Vitamin D levels; IL-6: Interleukin 6 levels; RCP: reactive C protein.

Introduction

(COVID-19 has caused more than 745 000 deaths worldwide [1]. Patients with COVID-19 show clinical clusters of severe respiratory illness manifestations including fever, nonproductive cough, dyspnea, myalgia, fatigue, abnormal leukocyte counts, and radiographic evidence of pneumonia, which are similar to the symptoms of previous SARS-CoV and MERS-CoV infections [2]. SARS-CoV-2 infection can remain asymptomatic or cause modest symptoms. Severely sick patients require hospital admission and about 20% of hospitalized patients will developed ARDS and require intensive care unit (ICU) treatment [3].

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ARDS, in patients with COVID-19 is also a life-threatening condition [4,5]. Although frequencies vary according to series, more than 40% of patients hospitalized because of COVID-19 pneumonia developed ARDS of which more than 50% ultimately died [6]. Vitamin D treatment has been identified as a potential strategy to prevent or treat COVID-19 [7]. More evidence is needed to establish the association between vitamin D levels and COVID-19 severity and mortality [8]. Therefore, studies are necessary to test this hypothesis.

Materials and Methods

This is a retrospective cohort study at a single ICU. Vitamin D normal values are considered if serum hydroxyvitamin D levels are 20-40 ng/ml. Vitamin D deficiency is considered if serum levels are less than 10 ng/ml, and insufficiency if serum levels are as 10-20 ng/ml.

Vitamin D deficiency was analyzed by a measurement of 25-hydroxycholecalciferol (immunoassay Diasorin Liaison XL Laboratory method) in the first 24- hour after COVID-19 testing. We included critically ill adult patients with COVID-19 who met ARDS criteria according to the Berlin definition [9] at the ICU from March to April 2020. The data that were collected within the first 24 hours of hospital admission were obtained from the anonymized database of hospital information systems. It was not registered if any of the patients previously used cholecalciferol. This study was approved by the Investigation Ethics Committee of the Hospital (PI-20-253) with a waiver of consent for use of identifiable data. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies. All variables were defined based on information from the UCM electronic health record (Epic; Epic Systems). COVID-19 test status was determined by any positive COVID-19 polymerase chain reaction test result. Basic descriptive statistics were reviewed for all variables. Fisher exact test was used for binary variables and the t test for continuous variables. Statistical significance was defined as $P < .05$. All tests were 2-tailed.

Results

A total of 35 patients with a median age of 60 years (33-76) were included in the study. A blood sample was drawn to analyze their vitamin D status within the first 24-hour after COVID-19 testing at hospital admission. All of them had a PaO2/FiO2 ratio below 100, 82.6% were intubated under invasive mechanical ventilation, 77% were under vasoactive drugs and 43% had Acute Kidney Injury (AKI). Vitamin D status was categorized as deficient for 14 participants (40%) and insufficient for 25 (71.4%). See table1.

Vitamin D deficiency was associated with lower levels of vitamin A , Zinc (P=0.019), albumin (P=0.026) and prealbumin (P=0.009). Overall, none of the studied variables were associated with vitamin D status: Vitamins B, C and E, mortality, ICU or hospital stay, necessity of vasoactive agents, intubation, prone position, AKI or renal replacement therapies (RRT), extracorporeal membrane oxygenation (ECMO), C-reactive protein (CRP), Dimer-D, Interleukin 6 levels (IL-6), ferritin levels, or bacterial superinfection.

Discussion

In this single-center retrospective cohort study, deficient vitamin D status was found in up to 40% in COVID-19 critically ill adult with ARDS. Patients with severe ARDS [10,11] or requiring ICU [12] are frequently severely vitamin D deficient [13]. In addition, low serum 25-hydroxyvitamin D (25[OH]D) levels in patients hospitalized with COVID-19 are associated with greater disease severity [14-16]. Vitamin D treatment has been found to decrease other viral respiratory infections, especially in persons with vitamin D deficiency [17]. Vitamin D modulates immune function through effects on dendritic cells and T cells [18], which may promote viral clearance and reduce inflammatory responses that produce symptoms. Given the low risks and low cost of vitamin D treatment, recent reporting has suggested that vitamin D treatment should be scaled [19]. Nevertheless, evidence of whether vitamin D deficiency is associated with COVID-19 infection and whether vitamin D treatment may help COVID-19 is lacking. In our study, vitamin D deficiency was a frequent event, but it was not associated with inflammation or outcome. Conversely, a pilot study with calcifediol has recently concluded that calcifediol may improve the clinical outcome of patients requiring hospitalization for COVID-19 [20].

Our study has also point out that Vitamin D deficiency was associated with other micronutrients low values as retinol and Zinc. Thus, Vitamin D deficiency may not be an isolated event in COVID-19 with ARDS and might be accompanied by other micronutrient deficiencies that should also be taken into account.

The study has several limitations, the studied population was critically ill adult with severe ARDS, so it is possible that other COVID patients less severe may have had another vitamin D status. The moment of the collection of the laboratory samples was within 24-hours of hospital admission, however, the time spent in the emergency room was not taken into account and it could have affected the results of Vitamin D status.

Conclusion

In this single-center retrospective cohort study, deficient vitamin D status was found in up to 40% in COVID-19 critically ill adult patients with ARDS. Vitamin D deficiency was associated with other low levels of micronutrients as retinol and Zinc. However, deficient vitamin D status was no associated with inflammation or outcome. Nonetheless, this was a small cohort study and vitamin D was measured in northern Spain in spring.

Authors Contribution

Conceptualization, T.M.T.I.; methodology, L.B.B.; software, L.B.B.; validation, T.M.T.I.,; formal analysis, L.B.B.; investigation, T.M.T.I.; data curation, L.B.B.; writing—original draft preparation, L.B.B.; writing—review and editing, T.M.T.I.; supervision, T.M.T.I. All authors have read and agreed to the published version of the manuscript.

Clinical Characteristics	COVID-19 ARDS (n=35)
Age (median, min-max, years)	60 (33–76)
Male (n, %)	26 (74.3)
SOFA score (median, min-max, points)	7 (2–15)
Intubation (n, %)	29 (82.6)
Prone position (n, %)	27 (77.14)
VV-ECMO (n, %)	3 (8.57)
VA-ECMO (n, %)	1 (2.86)
Noradrenaline (n, %)	25 (71.4)
Dobutamine (n, %)	2 (5.7)
CKD (n, %)	3 (8.57)
AKI (n, %)	15 (42.86)
CRRT (n, %)	1 (2.86)
IRR (n, %)	1 (2.86)
Bacterial superinfection (n, %)	13 (37.14)
DVT (n, %)	4 11.4)
PE (n, %)	1 (2.86)
ICU-LOS (median, min-max, days)	12 (1–112)
HOSP-LOS (median, min-max, days)	25 (1–185)
Mortality (n, %)	15 (27.8)
Vit. D (median, min-max, ng/mL, Normal values: 20-40)	12.8 (4–34.1)
Vit. D insufficiency (< 20 ng/mL, n, %)	25 (71.4)
Vit. D deficiency (< 10 ng/mL, n, %)	14 (40)
Vit. A (median, min-max, mg/L, Normal values: 0.3-0.6)	0.21 (0.035-0.9)
Zinc (median, min-max, mcg/dL, Normal values: 84-159)	73.7 (23.4–159)
Albumin (median, min-max, g/L, Normal values: 35-52)	27 (15.7–36.2)
Prealbumin (median, min-max, mg/dL, Normal values: 20 - 40)	8.2 (1.4–51.9)
CRP (median, min-max, mg/L, Normal values: 0 - 5)	160.1 (21.1–353.9)
IL-6 (median, min-max, pg/mL, Normal values: 0 – 6.4)	133.7 (4.6–1,537.7)
Ferritin (median, min-max, ng/mL, Normal values: 30 - 400)	1557.5 (254–44,553)
Dimer-D (median, min-max, ng/mL, Normal values: 0 - 500)	1050 (397–85,152)

Table 1: Characteristics of Patient Population.

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Conflict of Interest

The authors declare no conflict of interest.

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