

Vitamin D as a Key Modulator in Long COVID: Insights from a Mathematical Model

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Abstract

Vitamin D has been demonstrated to be a potent stimulator of mechanisms associated with pathogen clearance. Given its recognized efficacy against viral infections, the role of vitamin D supplementation during SARS-CoV-2 infection has been a subject of intense debate. This study aims to contribute to this ongoing discourse through the application of a qualitative phenomenological mathematical model, explicitly considering the role of vitamin D and its interactions with the innate immune system. We demonstrate that the influx and degradation of vitamin D may serve as potential control parameters for disease assessment and recovery.

Methods

Data were collected from hundreds of individuals during the 2020-2021 SARS-CoV-2 pandemic. We focused our analysis on 316 patients exhibiting symptoms consistent with Long COVID, characterized by persistent respiratory disturbances unequivocally linked to SARS-CoV-2 infection. Patients were consecutively recruited from November 20, 2020, to November 20, 2021, at the pneumology outpatient clinic of Abbiategrosso Hospital, with Long COVID confirmed following extensive evaluations.

Exclusion criteria involved contrast-enhanced chest CT scans to rule out pulmonary embolism, spirometry and plethysmography to exclude pre-existing Chronic Obstructive Pulmonary Disease (COPD), and treatment and exclusion of asthmatic and COPD patients from the Long COVID cohort. Respiratory pathophysiology assessments included carbon monoxide diffusion.

Variables examined encompassed complete blood count with differential, AST, ALT, Alkaline phosphatase, creatinine, Blood Urea Nitrogen, Electrolytes, Amylase, APTT, INR, fibrinogen, D-dimer, lymphocyte subpopulations, and vitamin D levels.

Patients were stratified into three severity groups based on criteria such as high-resolution chest CT scans performed at least 3 months post-recovery, blood gas analysis in stable conditions 3 months post-recovery, and carbon monoxide diffusion measurements.

Result

Patients with severe symptoms developed interstitial lung disease with ground-glass opacities, particularly at the lung bases, progressing to more severe pulmonary fibrosis, especially when pre-existing fibrotic lesions were present. Virtually all patients exhibited lesions consistent with recent scattered bronchopneumonic foci in both lung parenchyma, with these fibrotic lesions gradually regressing.

Respiratory pathophysiology in severely affected patients indicated a notable reduction in carbon monoxide diffusion, with values falling below 50% of theoretical values.

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Pletysmography consistently showed a mild reduction in residual volume, with values ranging from 66% to 89% of theoretical values.

In the most severely compromised patients post-SARS-CoV-2 recovery, ambient air oxygen levels (PO₂) were slightly reduced, ranging from 68 mmHg to 85 mmHg in blood gas analysis. However, pH, PCO₂, and bicarbonate levels remained within normal ranges.

Of all laboratory variables analyzed, vitamin D levels were the sole parameter exhibiting a precise correlation with the three dynamic severity scenarios.

Conclusion

To ascertain the strongest correlating parameter, a team of researchers, including mathematicians, statisticians, and computer scientists, examined vitamin D levels in relation to varying disease severities. Notably, the emergence of hysteresis phenomena at insufficient vitamin D levels was correlated with the onset of Long COVID syndrome, corroborating recent clinical evidence. This study underscores the potential significance of vitamin D as a modulator in Long COVID and warrants further investigation.