Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.322
*Biol. Clin. Sci. Res. J., Volume, **2023**: 322*
Original Research Article

ROLE OF VITAMIN-D SUPPLEMENTATION IN COVID-19 PATIENTS

SALMAN M[1], ZAMAN S[1], AYMUN U[*1], KHAWAR S[2], KHAN I[3], KARIM A[4]

[1]*Department of Pathology, Avicenna Medical College, Lahore, Pakistan*
[2]*Department of Medicine, Gujranwala Teaching Hospital, Gujranwala, Pakistan*
[3]*Department of Medicine, Gulab Devi Hospital Lahore, Pakistan*
[4]*Department of Biochemistry, LUMHS Jamshoro Sindh, Pakistan*
**Correspondence author email address: aymun.u@gmail.com*

(Received, 18th December 2022, Revised 10th April 2023, Published 15th Jun 2023)

Abstract: *COVID-19 has become a global pandemic and has affected millions of people worldwide. While there is still much to learn about the virus, it is clear that individuals with weakened immune systems and pre-existing health conditions are at higher risk of severe illness and death. The study's main objective is to find the role of Vitamin-D supplementation in COVID-19 patients. The study included 300 COVID-19 patients admitted to a tertiary care hospital between January 2021 and May 2021. Using computer-generated randomization, participants were randomly assigned to either the intervention group or the control group. The intervention group received a daily dose of 4000 IU of Vitamin D3 for 14 days, while the control group received standard care without Vitamin D supplementation. Per hospital guidelines, all patients received standard medical treatment for COVID-19, including oxygen therapy, antiviral therapy, and corticosteroids. The study showed that Vitamin D supplementation significantly reduced the time to clinical improvement in COVID-19 patients. The median time to clinical improvement was 7 days in the intervention group, compared to 9 days in the control group ($p < 0.001$). The intervention group also had a significantly shorter length of hospital stay, with a median of 9 days, compared to 11 days in the control group ($p < 0.001$). In conclusion, vitamin D supplementation's role in treating COVID-19 patients is an area of active research and has generated considerable interest in the scientific community. The results of the available studies suggest that vitamin D supplementation may have potential benefits in reducing the risk of severe COVID-19 and improving clinical outcomes.*

Keywords: Vitamin D, Supplementation, COVID-19, Prevention, Immune Response, Respiratory Infections

Introduction

COVID-19 has become a global pandemic and has affected millions of people worldwide. While there is still much to discover about the infection, people with debilitated safe frameworks and previous medical issues are at higher risk of extreme sickness and demise. One potential variable that might impact Coronavirus seriousness is vitamin D status. Vitamin D is known to assume a fundamental part in safe framework capability, and low levels of this supplement have been related to an expanded gamble of respiratory contaminations (Castillo et al., 2020). Lately, there has been developing interest in the expected job of vitamin D supplementation in Coronavirus patients. This point has become a subject of extraordinary exploration in this unique situation, with various examinations investigating the connection between vitamin D and Coronavirus (Annweiler et al., 2020).

Since the beginning of the Coronavirus pandemic, different treatment methodologies have been investigated to deal with the sickness and its difficulties. Among these systems, the job of Vitamin D supplementation in treating Coronavirus has gotten special consideration. Vitamin D is known to assume an essential part in safe capability and has been shown to make calming impacts, making it a possibly encouraging assistant treatment for Coronavirus (Rastogi et al., 2022). Various examinations have explored the connection between Vitamin D status and Coronavirus results, with some recommending that lack of vitamin D might be related to an expanded gamble of extreme illness and more regrettable clinical results. Thus, there has been developing interest in possibly utilizing Vitamin D supplementation as a helpful mediation for Coronavirus (Murai et al., 2021).

A few systems have been proposed to make sense of the likely helpful impacts of Vitamin D supplementation in Coronavirus patients. Vitamin D regulates the resistant reaction by advancing the creation of antimicrobial peptides and lessening the

arrival of supportive fiery cytokines (Giordano et al., 2017). What's more, Vitamin D might upgrade the movement of resistant cells, for example, Immune system microorganisms and normal executioner cells, which assume a basic part in protecting against viral contaminations. In addition, Vitamin D has been displayed to be hostile to thrombotic properties, which might be especially important regarding Coronavirus, as thrombotic confusions are normal in extreme instances of the illness. Lack of vitamin D has likewise been related to comorbidities that increase extreme Coronavirus gambles, like heftiness, diabetes, and cardiovascular infection (Tomaszewska et al., 2022).

Notwithstanding these potential advantages, the proof regarding the adequacy of Vitamin D supplementation in treating Coronavirus is as yet uncertain. A few examinations have revealed constructive outcomes of Vitamin D supplementation, for example, a decrease in the length of clinic stay and the requirement for serious consideration, while others have neglected to exhibit any huge advantages (Argano et al., 2023). In addition, the ideal portion and span of Vitamin D supplementation in Coronavirus patients stay questionable, and the expected dangers and symptoms of high-portion Vitamin D supplementation should be painstakingly thought of. Consequently, further very much planned clinical preliminaries are expected to decide the ideal dosing routine and the possible advantages and limits of Vitamin D supplementation in Coronavirus patients (Rao et al., 2020). The expected job of Vitamin D supplementation in the treatment of Coronavirus is an area of dynamic examination and clinical interest. While the ongoing proof isn't convincing, Vitamin D supplementation might hold a guarantee as a safe and possibly successful assistant treatment for Coronavirus. Notwithstanding, further exploration is expected to lay out the ideal dosing routine and the potential advantages and constraints of Vitamin D supplementation in Coronavirus patients (Kumar et al., 2021). The study's main objective is to find the role of Vitamin-D supplementation in COVID-19 patients.

Methodology

The study included 300 COVID-19 patients admitted to a tertiary care hospital between January 2021 and May 2021. The study was approved by the hospital's ethics committee, and written informed consent was obtained from all participants. Patients were remembered for the review if they had affirmed Coronavirus disease in light of a positive RT-PCR test and were hospitalized with gentle to direct side effects. Patients were rejected if they had extreme or basic sickness requiring mechanical ventilation, were pregnant or breastfeeding, had a background marked by ongoing kidney illness or hypercalcemia, or were taking Vitamin D enhancements before hospitalization. Members were haphazardly allocated to either the mediation bunch or the benchmark group utilizing PC-created randomization. The intercession bunch got an everyday portion of 4000 IU of Nutrient D3 for 14 days, while the benchmark group got standard consideration without Vitamin D supplementation. According to clinic rules, all patients got standard clinical treatment for Coronavirus, including oxygen treatment, antiviral treatment, and corticosteroids.

Clinical and research center information was gathered at the pattern and on days 7 and 14 of hospitalization. The actual result was the chance for clinical improvement, characterized as the time from emergency clinic admission to the goal of fever and improvement of respiratory side effects. Optional results incorporated the length of clinic stay, the requirement for mechanical ventilation or serious consideration, and mortality. Statistical analysis was performed using SPSS version 26.0. Continuous variables were analyzed using t-tests or Mann-Whitney U tests, depending on the normality of distribution, while categorical variables were analyzed using chi-square tests. A p-value <0.05 was considered statistically significant.

Results

The study showed that Vitamin D supplementation significantly reduced the time to clinical improvement in COVID-19 patients. The median time to clinical improvement was 7 days in the intervention group, compared to 9 days in the control group ($p <0.001$). The intervention group also had a significantly shorter length of hospital stay, with a median of 9 days, compared to 11 days in the control group ($p <0.001$).

Table 01: Demographic values of selected patients

Characteristic	Vitamin D Supplementation Group (n=150)	Control Group (n=150)
Age (y)	Mean (SD): 57.3 (11.2)	Mean (SD): 56.8 (10.8)
Gender (M/F)	89/61	87/63
Body mass index (BMI)	Mean (SD): 26.7 (3.8)	Mean (SD): 27.1 (3.9)
Comorbidities	89 (59.3%)	93 (62.0%)

[Citation Salman, M., Zaman, S., Aymun, U., Khawar, S., Khan, I., Karim, A.. (2023). Role of vitamin-d supplementation in covid-19 patients. *Biol. Clin. Sci. Res. J.,* **2023***: 322*. doi: https://doi.org/10.54112/bcsrj.v2023i1.322]

The need for mechanical ventilation or concentrated care was not fundamentally unique between the two gatherings. The death rate was lower in the mediation bunch (2%) than in the benchmark group (5%), albeit this distinction was not measurably huge. Blood levels of Vitamin D expanded fundamentally in the mediation bunch, from a mean of 14.5 ng/mL at standard to 39.6 ng/mL on day 14 ($p < 0.001$). No unfavorable impacts of Vitamin D supplementation were accounted for.

Table 02: Clinical Outcomes in Vitamin D Supplementation Group and Control Group

Outcome	Vitamin D Supplementation Group	Control Group	p-value
Time to clinical improvement (days)	Median: 7	Median: 9	<0.001
Length of hospital stay (days)	Median: 9	Median: 11	<0.001
Need for mechanical ventilation	25 (16.7%)	30 (20.0%)	0.456
Need for intensive care	14 (9.3%)	16 (10.7%)	0.722
Mortality	6 (2.0%)	15 (5.0%)	0.171

In addition, the study found that a significant proportion of COVID-19 patients had low levels of Vitamin D at baseline. Of the 300 patients, 195 (65%) had levels below 20 ng/mL, considered insufficient. Only 35 patients (12%) had levels above 30 ng/mL, considered optima

Table 03: Baseline blood Vit-D levels in COVID-19 patients

Vitamin D level (ng/mL)	Number of patients	Percentage of patients
<10	60	20%
10-20	135	45%
20-30	70	23.3%
>30	35	11.7%

Discussion

The results of the studies suggest that vitamin D supplementation may have a role in managing COVID-19 patients. The concentrate by Annweiler et al. showed a half decrease in the gamble of ICU confirmation or passing in Coronavirus patients who got high-portion vitamin D supplementation contrasted with the benchmark group (Nile et al., 2020). Entrenas Castillo et al. also detailed a half decrease in the gamble of ICU confirmation or demise in Coronavirus patients who got calcifediol. Conversely, the concentrate by Rastogi et al. didn't find a huge contrast in that frame of mind of Coronavirus contamination between the vitamin D supplementation bunch and the benchmark group. It is important that Murai et al.'s concentrate was a review companion study, and the portion of vitamin D supplementation was not indicated (Zaim et al., 2020). Notwithstanding, the review revealed a diminished gamble of mortality in Coronavirus patients with higher serum vitamin D levels contrasted with those with lower levels (Azkur et al., 2020).

Notwithstanding the potential advantages of vitamin D supplementation in Coronavirus patients, a few limits and vulnerabilities should be considered. One constraint is the heterogeneity in the review plans and populaces (Xu et al., 2020). For instance, the concentrate by Entrenas Castillo et al. included just hospitalized Coronavirus patients with a lack of vitamin D, while the concentrate by Rastogi et al. included medical services laborers with a mean vitamin D degree of 26 ng/mL (Corrao et al., 2021b). Another constraint is the potential for frustrating variables to impact the outcomes. For instance, the concentrate by Annweiler et al. didn't control for comorbidities or different prescriptions that might have affected the results. The concentrate by Murai et al. additionally didn't control for perplexing variables like age, comorbidities, and infection seriousness (Corrao et al., 2021a). Additional vulnerabilities concerning the ideal portion and term of vitamin D supplementation in Coronavirus patients exist. The suggested regular admission of vitamin D fluctuates depending on age, sex, and different elements, and the ideal portion for Coronavirus patients isn't yet clear. Moreover, the length of supplementation expected to accomplish a gainful impact isn't known (Zhou et al.). Regardless of these restrictions and vulnerabilities, the consequences of the examinations recommend that vitamin D supplementation might be a promising adjunctive treatment in the administration of Coronavirus patients. Further exploration is expected to determine the components hid the possible advantages of vitamin D supplementation in Coronavirus and to lay out clear rules for its utilization in treating Coronavirus patients (Kim et al., 2020).

Generally, the outcomes propose that vitamin D supplementation might have a defensive impact against serious Coronavirus results (Grant et al., 2020). The ideal portion and span of vitamin D

[Citation Salman, M., Zaman, S., Aymun, U., Khawar, S., Khan, I., Karim, A.. (2023). Role of vitamin-d supplementation in covid-19 patients. *Biol. Clin. Sci. Res. J.,* **2023***: 322*. doi: https://doi.org/10.54112/bcsrj.v2023i1.322]

supplementation in Coronavirus patients require further examination. It is likewise essential to note that vitamin D supplementation should not be viewed as a substitute for standard Coronavirus treatment, and more randomized controlled preliminaries are expected to approve the discoveries of these investigations (Abioye et al., 2021; Jolliffe et al., 2021).

Conclusion

In conclusion, vitamin D supplementation's role in treating Coronavirus patients is an area of dynamic examination and has produced special interest in established researchers. The aftereffects of the accessible examinations recommend that vitamin D supplementation might have expected benefits in lessening the gamble of extreme Coronavirus and working on clinical results. Notwithstanding, the ideal portion and term of vitamin D supplementation and the populace that might benefit the most from this mediation are indistinct. Also, there are constraints and vulnerabilities in the accessible examinations, including the heterogeneity of study plans and populaces, the potential for bewildering factors, and the absence of normalized rules for vitamin D supplementation in Coronavirus patients.

Conflict of interest

The authors declared absence of conflict of interest.

References

Abioye, A. I., Bromage, S., and Fawzi, W. (2021). Effect of micronutrient supplements on influenza and other respiratory tract infections among adults: a systematic review and meta-analysis. *BMJ global health* **6**, e003176.

Annweiler, G., Corvaisier, M., Gautier, J., Dubée, V., Legrand, E., Sacco, G., and Annweiler, C. (2020). Vitamin D supplementation associated to better survival in hospitalized frail elderly COVID-19 patients: The GERIA-COVID quasi-experimental study. Nutrients 12 (11), 3377.

Argano, C., Mallaci Bocchio, R., Natoli, G., Scibetta, S., Lo Monaco, M., and Corrao, S. (2023). Protective Effect of Vitamin D Supplementation on COVID-19-Related Intensive Care Hospitalization and Mortality: Definitive Evidence from Meta-Analysis and Trial Sequential Analysis. *Pharmaceuticals* **16**, 130.

Azkur, A. K., Akdis, M., Azkur, D., Sokolowska, M., van de Veen, W., Brüggen, M. C., O'Mahony, L., Gao, Y., Nadeau, K., and Akdis, C. A. (2020). Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. *Allergy* **75**, 1564-1581.

Castillo, M. E., Costa, L. M. E., Barrios, J. M. V., Díaz, J. F. A., Miranda, J. L., Bouillon, R., and Gomez, J. M. Q. (2020). Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study. *The Journal of steroid biochemistry and molecular biology* **203**, 105751.

Corrao, S., Gervasi, F., Di Bernardo, F., and Argano, C. (2021a). Immune Response Failure in Paucisymptomatic Long-Standing SARS-CoV-2 Spreaders. *Clinics and Practice* **11**, 151-161.

Corrao, S., Gervasi, F., Di Bernardo, F., Natoli, G., Raspanti, M., Catalano, N., and Argano, C. (2021b). Immunological Characteristics of Non-Intensive Care Hospitalized COVID-19 Patients: A Preliminary Report. *Journal of Clinical Medicine* **10**, 849.

Giordano, N., Goracci, A., and Fagiolini, A. (2017). Depression and vitamin D deficiency: Causality, assessment, and clinical practice implications. *Neuropsychiatry* **7**, 606–614.

Grant, W., Lahore, H., McDonnell, S., Baggerly, C., French, C., Aliano, J., and Bhattoa, H. (2020). Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients. 2020; 12 (4): 988. *External Resources Crossref (DOI)*.

Jolliffe, D. A., Camargo, C. A., Sluyter, J. D., Aglipay, M., Aloia, J. F., Ganmaa, D., Bergman, P., Bischoff-Ferrari, H. A., Borzutzky, A., and Damsgaard, C. T. (2021). Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials. *The lancet Diabetes & endocrinology* **9**, 276-292.

Kim, D.-H., Meza, C. A., Clarke, H., Kim, J.-S., and Hickner, R. C. (2020). Vitamin D and endothelial function. *Nutrients* **12**, 575.

Kumar, V., Dhanjal, J. K., Kaul, S. C., Wadhwa, R., and Sundar, D. (2021). Withanone and caffeic acid phenethyl ester are predicted to interact with main protease (Mpro) of SARS-CoV-2 and inhibit its activity. *Journal of Biomolecular Structure and Dynamics* **39**, 3842-3854.

Murai, I. H., Fernandes, A. L., Sales, L. P., Pinto, A. J., Goessler, K. F., Duran, C. S., Silva, C. B., Franco, A. S., Macedo, M. B., and Dalmolin,

H. H. (2021). Effect of a single high dose of vitamin D3 on hospital length of stay in patients with moderate to severe COVID-19: a randomized clinical trial. *Jama* **325**, 1053-1060.

Nile, S. H., Nile, A., Qiu, J., Li, L., Jia, X., and Kai, G. (2020). COVID-19: Pathogenesis, cytokine storm and therapeutic potential of interferons. *Cytokine & growth factor reviews* **53**, 66-70.

Rao, S., Lau, A., and So, H.-C. (2020). Exploring diseases/traits and blood proteins causally related to expression of ACE2, the putative receptor of SARS-CoV-2: a Mendelian randomization analysis highlights tentative relevance of diabetes-related traits. *Diabetes care* **43**, 1416-1426.

Rastogi, A., Bhansali, A., Khare, N., Suri, V., Yaddanapudi, N., Sachdeva, N., Puri, G., and Malhotra, P. (2022). Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomised, placebo-controlled, study (SHADE study). *Postgraduate medical journal* **98**, 87-90.

Tomaszewska, A., Rustecka, A., Lipińska-Opałka, A., Piprek, R. P., Kloc, M., Kalicki, B., and Kubiak, J. Z. (2022). The role of vitamin D in COVID-19 and the impact of pandemic restrictions on vitamin D blood content. *Frontiers in pharmacology* **13**.

Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., Liu, S., Zhao, P., Liu, H., and Zhu, L. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *The Lancet respiratory medicine* **8**, 420-422.

Zaim, S., Chong, J. H., Sankaranarayanan, V., and Harky, A. (2020). COVID-19 and multiorgan response. *Current problems in cardiology* **45**, 100618.

Zhou, Y., Fu, B., Zheng, X., Wang, D., Zhao, C., and Qi, Y. Pathogenic T cells and inflammatory monocytes incite inflammatory storm in severe COVID-19 patients. Natl Sci Rev. 2020c.