Effect of Vitamin D Supplementation on Post-COVID-19 Manifestations in Menoufia University Hospitals: A Randomized Controlled Clinical Trial

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Abstract

Background: The aftermath of the COVID-19 pandemic has given rise to a diverse array of challenges impacting multiple facets of daily life. Vitamin D, renowned for its immunomodulatory properties, has been implicated in mitigating viral infections, preventing complications, and arresting the progression of chronic conditions. **Objectives:** To evaluate the effect of vitamin D supplementation in ameliorating post-COVID-19 symptoms. **Methods:** A randomized-controlled clinical trial was conducted on 111 post-COVID-19 patients recruited from the post-COVID-19 Outpatient Clinic at Menoufia University Hospital between October 2021 and June 2022. Before the intervention, baseline data, detailed medical history, and clinical assessments were collected. Additionally, serum vitamin D levels were measured in all patients. Subsequently, participants were randomly assigned to a 2-month supplementation regimen, either the vitamin D group, receiving a daily oral dose of vitamin D (2000 IU/tablet), or a visually identical placebo. **Results:** Among patients with insufficient vitamin D levels, approximately 75.7% experienced more than 3 post-COVID-19 symptoms. A notable negative correlation was observed between the frequency of post-COVID-19 symptoms and vitamin D levels (R=-0.505, P-value< 0.001). After a 2-month intervention with vitamin D, compared to the placebo, there was a significant improvement in various symptoms such as fatigue, sleep disturbance, lack of concentration, cough, myalgia, arthralgia, and hair loss (P-value<0.001). **Conclusion:** This study establishes a significant connection between vitamin D deficiency and persistent post-COVID-19 symptoms, emphasizing the beneficial role of vitamin D in relieving symptoms. The findings support the routine assessment of vitamin D levels in individuals with post-COVID-19 symptoms, with a recommendation for vitamin D supplementation in cases of deficiency.

Keywords: COVID; Deficiency; Improvement; Vitamin D

Introduction

Individuals recovering from acute COVID-19 often report persistent symptoms, leading to a condition commonly referred to as chronic or long COVID-19, more recently labeled post-COVID-19

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syndrome. This phenomenon encompasses a broad spectrum of physical and mental health repercussions experienced by certain individuals beyond 4 weeks following SARS-CoV-2 infection, including those who had an initially mild or asymptomatic acute infection. [1]

The spectrum of persistent complaints associated with this condition is broad, encompassing symptoms such as cough, mild fever, lethargy, dyspnea, chest pain, headache, neuro-cognitive troubles, myalgia, weakness, gastrointestinal issues, skin rash, metabolic abnormalities, thrombo-embolic disorders, and mental health challenges, including hopelessness and other mental diseases. [2]

Amidst the challenges posed by post-COVID-19 conditions, the role of vitamin D has garnered significant attention. Vitamin D is acknowledged for its crucial function in fortifying the immune system and regulating immune-modulatory mechanisms.

Beyond its immunological role, vitamin D is essential for maintaining healthy bones, teeth, and muscles. It also plays a regulatory role in blood sugar, heart and blood vessels, and the respiratory system, including the lungs and airways. **[3]**

Numerous studies have underscored the critical importance of maintaining optimal serum levels of vitamin D in mitigating viral infections and their complications.

This extends to reducing the incidence and progression of various chronic conditions, encompassing human immunodeficiency virus, hepatitis B and C viruses, pneumonia, autoimmune disorders, cancers, and metabolic disorders. [4]

Research indicates a negative association between serum vitamin D levels and COVID-19 contagion rates, with evidence suggesting that improving vitamin D status through supplementation may reduce clinical hazards associated with COVID-19. [5] Evidence-based studies have suggested that enhancing vitamin D status through supplementation may mitigate the clinical hazards associated with COVID-19 and alleviate post-COVID-19 sequelae.

This insight has prompted further exploration into the potential benefits of vitamin D supplementation as part of COVID-19 management strategies. **[6]**

The study aims to evaluate the effect of vitamin D supplementation in ameliorating post-COVID-19 symptoms.

Patient and methods

Research design: This research utilized a randomized controlled clinical trial involving post-COVID-19 patients with vitamin D deficiency.

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Study time and setting Participants were recruited from the post-COVID-19 Outpatient Clinic at Menoufia University Hospital between October 2021 and June 2022.

Study population: Based on past research conducted by Padi *et al.*, [7] who reported the correlation between vitamin D deficiency and COVID-19 symptoms to be -0.42, sample size had been calculated at power 80% and confidence interval 95% and it was 55 patients.

To conduct a clinical trial an equal number was recruited to serve as a placebo group giving a final number of 84. Accounting for a dropout of 25%, a total of 112 patients were recruited. One patient was dropped giving back a total of 111 patients to be analyzed.

Eligible patients were those with persistent symptoms lasting more than 4 weeks post-COVID-19 infection, attending Menoufia University Hospital's post-COVID-19 outpatient clinic.

Inclusion criteria required a confirmed positive COVID-19 diagnosis through methods like positive polymerase chain reaction (PCR) test, serology assay (ELISA) detecting IgG, or a chest computed tomography (CT) scan indicating bilateral multifocal ground-glass opacities with at least 50% lung involvement.

Exclusion criteria applied to patients with conditions affecting vitamin D levels, such as chronic liver or renal diseases, immune deficiency, malignancy, those with multiorgan system effects or post-COVID-19 hospitalization, and those with declining participation.

Tools of the study: After enrolment, eligible patients were assigned to randomize in a 1:1 into the vitamin D group supplementation or the placebo group using a computer-generated code, in bloc sizes of 2. (GraphPad Quick Cals, La Jolla, California, USA). The randomization schedule was designed by an independent person who also evaluated the packaging and labeling procedure to ensure blindness.

The vitamin D group (n=55) received a daily maintenance dose of 2000 IU per tablet (2 tablets/day), while the placebo group (n=56) received visually identical placebos. Both groups underwent a 2-month treatment period, then clinically followed up after 2 months. [8] The control group later receives vitamin D supplementation for ethical considerations.

The selected dose falls within the recommended range effective in promoting vitamin D sufficiency. [8] The vitamin D and placebo were identical in color, taste, smell, consistency, and container. Both were labeled by a staff member not participating

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in the study, and allocation blindness was maintained until the final statistical analysis.

Throughout the study, all investigators and patients were blinded. After the study was completed, the randomization codes were opened.

Structured interviews, medical history, and clinical assessments were conducted using a validated Arabic questionnaire before the intervention. The questionnaire covered identification data, socioeconomic status using the socioeconomic scoring system developed by El-Gilany, *et al.* [9], medical history, and post-COVID-19 symptoms severity using the Edmonton Symptom Assessment System (ESAS).

The scale from 1-10, with 1 indicating very mild symptoms and 10 indicating very severe symptoms. [10] The symptoms are categorized into various domains by the Centers for Disease Control and Prevention (CDC).

The Arabic questionnaire underwent translation, validation, and revision by a panel of three experts (two professors of family medicine and one professor of community medicine).

The reliability of the questionnaire, evaluated using SPSS version 20 and Cronbach's alpha (r = 0.936), indicated a high level of internal consistency.

General and physical examinations were conducted, and approximately 2 ml of blood was withdrawn for the assessment of 25-hydroxy vitamin D levels in the serum using the Enzyme-Linked Immunosorbent Assay (ELISA).

The samples were forwarded to the clinical pathology research laboratory at Menoufia University Hospital. Vitamin D levels were categorized as normal (> 30 ng/dl) or deficient (< 30 ng/dl) following the criteria established by Pagana *et al.* [11]

All study groups received their prescribed medication and were consistently contacted via phone calls and SMS messages every 2 weeks to emphasize medication adherence. Vitamin D levels for the case group were measured 2 months after the start of the intervention.

Additionally, all participants completed the third section of the questionnaire (post-COVID-19 symptoms severity), which was initially filled out before the start of treatment. This assessment aimed to evaluate changes in symptom severity based on the ESAS scale.

Data management: Data were coded, entered, and analyzed using Statistical Package for Social Sciences software, version 21 (SPSS Inc., Chicago, IL). Descriptive results were expressed as

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frequency, percentages, and mean±S.D. Statistically significant differences were considered at P-values≤0.05. Pearson chi-square tested significant relationships between categorical variables, while the independent sample t-test examined differences in means between groups.

Pearson's correlation determined the correlation between parametric quantitative variables, and the Wilcoxon signed-rank test (Z test), a non-parametric test, was used to assess differences between two dependent samples. Results were presented in tables and graphs.

Ethical consideration: The study obtained ethical approval from the Research Ethics Committee of the Faculty of Medicine, Menoufia University, with IBR approval number and date 8/2021 FAML 26. Informed written consent was diligently obtained from each participant after providing a comprehensive explanation of the research goals and potential benefits. The confidentiality of all collected data was strictly maintained for research purposes.

Results

The study included 111 patients with a mean age of (35.36±6.73) years. The majority were female (63.9%), mainly non-smokers, and approximately (77.5%) had two or more comorbidities. Additionally, (83.8%) had a BMI of less than 30 kg/m2. Of the total participants, (75.7%) reported experiencing three or more persistent post-COVID-19 symptoms while (24.3%) reported less than three persistent symptoms (Table 1).

A notable negative correlation was identified between the frequency of post-COVID-19 symptoms and vitamin D levels, indicating that an increase in vitamin D levels corresponded to a decrease in the frequency of post-COVID-19 symptoms (R= -0.505, P< 0.001). (Figure 1).

In the subgroup of post-COVID-19 patients receiving 2 months of vitamin D supplementation (55 cases), a significant improvement was observed in cardio-respiratory and most neuropsychiatric symptoms, including fatigue, sleep disturbance, lack of concentration, poor memory, headache, anosmia, and loss of taste (P< 0.05). (Table 2).

Furthermore, a notable enhancement in symptoms like loss of appetite (P=0.029), diarrhea (P=0.003), myalgia (P< 0.001), arthralgia (P< 0.001), and skin rash/hair loss (P< 0.001) was noted after the 2-month intervention with vitamin D compared to the placebo. (Table 3).

Before the intervention, fatigue and myalgia were the most prevalent post-COVID-19 symptoms among participants (76.1% and 70.3%), followed by sleep

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disturbance and poor memory (69.7% and 63.2%) (Figure 2a). Subsequently, there was an improvement in these post-COVID-19 symptoms after 2 months of receiving vitamin D supplementation (39.4%, 31.2%, 36.4%, and 24.1%) (Figure 2b).

Discussion

Post-recovery manifestations have become a growing concern in patients who have survived COVID-19. This research specifically focuses on post-COVID-19 symptoms and aims to explore the impact of vitamin D on different manifestations arising after COVID-19.

The study indicated that approximately 75.7% of the participants had more than three persistent post-COVID-19 symptoms. This aligns with studies conducted in Turkey and Italy by Kayaaslan *et al.,* [12] and Carfi *et al.,* [13] respectively, reporting that more than half of the patients (51.3% and 55.2%, respectively) had three or more persistent post-COVID-19 symptoms. In contrast, a study by Whitaker *et al.,* [14] in England found that about 37.7% of post-COVID-19 patients experienced at least one or two symptoms, while 14.8% experienced three or more symptoms.

The current study revealed a negative correlation between the frequency of post-COVID-19 symptoms and vitamin D levels, indicating that more severe and frequent post-COVID-19 symptoms were observed among individuals with deficient vitamin D levels.

These findings align with a systematic review and meta-analysis conducted by Bassatne *et al.,* [15] reporting an association between vitamin D deficiency and increased severity of COVID-19 infection and post-COVID-19 conditions.

Patients with serum 25(OH)D levels below 30ng/ml were found to be more likely to test positive for COVID-19 and had an elevated risk of developing post-COVID-19 sequelae.

Additionally, studies conducted in Ireland by Townsend *et al.,* [16] and in Italy by Fernandes *et al.,* [17] explored the relationship between vitamin D deficiency and the incidence of different symptoms such as fatigue, decreased exercise tolerance, and physical performance after COVID-19 infection. In contrast, the study by Daneshkhah *et al.,* [18] in England reported no significant relationship between vitamin D deficiency and the rate of occurrence of post-COVID-19 sequelae.

It's essential to note that findings in the field are evolving, and different studies may show varying results, possibly influenced by factors such as sample size, population demographics, and methodology.

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In this study, the most prevalent persistent post-COVID-19 symptoms among participants were related to the neuropsychiatric system, including fatigue, poor memory, lack of concentration, and headache.

Musculoskeletal symptoms, such as myalgia and arthralgia, ranked as the second most common symptoms, followed by cardio-respiratory system symptoms like cough and palpitation. Skin rash and hair loss were frequently reported as general symptoms.

These findings align closely with the results reported in a review article by Yong, [19] based on PubMed databases, and a study by Pavli *et al.,* [20] which both highlighted various persistent symptoms after COVID-19, such as memory loss, anosmia, fatigue, and various neuropsychiatric sequelae, including depression, anxiety, and post-traumatic stress disorder.

On the contrary, a study in Egypt by Elgendy *et al.,* [21] reported that diarrhea and loss of appetite were the most common post-COVID symptoms in 74% of participants, followed by fever, an increase in heart rate, shortness of breath, and muscle pain.

The study results indicated a significant improvement in various post-COVID-19 symptoms among patients who received vitamin D supplementation for 2 months.

This suggests that vitamin D supplementation can be utilized to enhance health outcomes following COVID-19. The study by Gönen *et al.,* [22] conducted in Turkey demonstrated that aggressively raising serum vitamin D concentrations to a mean value near 35 ng/mL within 4 weeks for COVID-19 patients significantly reduced the mortality rate and post-COVID-19 symptoms. Similarly, the study by Castillo *et al.,* [23] in Spain found that treating hospitalized COVID-19 patients with a high dose of calcifediol for a long period after COVID-19 significantly reduced the need for admission to the Intensive Care Unit (ICU) and lowered the risk of developing post-COVID-19 sequelae.

These findings are in contrast with a pilot clinical trial conducted in Spain by Caballero-García *et al.,* [24] which reported slight, non-significant improvements in physical tests with cholecalciferol treatment compared to placebo over 6 weeks. Additionally, the interventional clinical trial in Italy by Fernandes *et al.,* [17] where patients receiving a single dose of 200,000 IU of vitamin-D3 or placebo during the post-COVID-19 period did not show significant differences in various post-COVID-19 symptoms at the 6-month follow-up. So, both previous studies reported no improvement in various post-COVID-19 symptoms after vitamin D supplementation in the post-COVID-19 period.

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Vitamin D deficiency was prevalent among post-COVID-19 patients, with an observed association with symptom frequency. Supplementation proved effective in symptom improvement.

Further studies are recommended to understand the relationship between drug use, especially vitamin D, and the improvement of post-COVID symptoms. In conclusion, if our data is confirmed in large interventional randomized-controlled trials, it may suggest that vitamin D supplementation could serve as a potential preventive strategy in reducing the burden of COVID-19 sequela.

Study limitation

The current study acknowledges certain limitations. Specifically, we only included patients managed at home, excluding those requiring ICU admission or previously hospitalized due to COVID-19 infection. Additionally, data on vitamin D levels during acute COVID-19 infection were not recorded. Understanding whether vitamin D deficiency was pre-existing or occurred due to illness would provide valuable insights.

Conclusion

Post-COVID-19 conditions were widespread among Menoufia University Hospital attendees. Vitamin D deficiency was common among post-COVID-19 patients, and an association with symptom frequency was observed.

Vitamin D supplementation demonstrated effectiveness in symptom improvement. Though promising, confirmation through large randomized-controlled trials is crucial. If validated, vitamin D supplementation could serve as a potential preventive strategy for mitigating COVID-19 sequelae.

Declarations

Competing interests: There is no conflict of interest to declare**.**

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References

1. Alkodaymi MS, Omrani OA, Fawzy NA, *et al.* Prevalence of post-acute COVID-19 syndrome symptoms at different follow-up periods: a systematic review and meta-analysis. Clinical Microbiology and Infection. 2022; 28(5):657-666.
2. Dasgupta A, Kalhan A, Kalra S. Long-term complications and rehabilitation of COVID-19 patients. J Pak Med Assoc. 2020; 70(5): S131-135.
3. Banerjee A, Ganguly U, Saha S, *et al.* Vitamin D and immuno-pathology of

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COVID-19: many interactions but uncertain therapeutic benefits. Expert review of anti-infective therapy. 2021; 19(10):1245-1258.

4. Infante M, Ricordi C, Sanchez J, *et al.* Influence of vitamin D on islet autoimmunity and beta-cell function in type 1 diabetes. Nutrients. 2019; 11(9): 2185-2215.
5. Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging clinical and experimental research. 2019; 32(7): 1195-1198.
6. Ahmad A, Heumann C, Ali R, *et al.* Mean Vitamin D levels in 19 European Countries & COVID-19 Mortality over 10 months. MedRxiv. 2021; 3(2):1-12.
7. Padhi S, Suvankar S, Panda VK, *et al.* Lower levels of vitamin D are associated with SARS-CoV-2 infection and mortality in the Indian population: an observational study. International immunopharmacology. 2020; 88(1):107001.
8. Rusińska A, Płudowski P, Walczak M, *et al.* Vitamin D supplementation guidelines for the general population and groups at risk of vitamin D deficiency in Poland—recommendations of the Polish Society of Pediatric Endocrinology and Diabetes and the expert panel with participation of national specialist consultants and representatives of scientific societies—2018 update. Frontiers in Endocrinology. 2018; 9(1): e246-e256.
9. El-Gilany A, El-Wehady A, El-Wasify M. Updating and validation of the socioeconomic status scale for health research in Egypt. Eastern Mediterranean health journal. 2012; 18(9): 962-968.
10. Moro C, Brunelli C, Miccinesi G, *et al.* Edmonton symptom assessment scale: Italian validation in two palliative care settings. Supportive care in cancer. 2006; 14: 30-37.
11. Pagana KD, Pagana TJ, Pagana TN. Editors. Mosby's Diagnostic & Laboratory Test Reference. 14th Ed. St. Louis, Mo: Elsevier, 2019; 325-325.
12. Kayaaslan B, Eser F, Kalem AK, *et al.* Post- COVID syndrome: A single-center questionnaire study on 1007 participants recovered from COVID-19. Journal of medical virology. 2021; 93(12): 6566-6574.
13. Carfì A, Bernabi R, Landi F. Persistent symptoms in patients after acute COVID-19. Jama. 2020; 324(6): 603-605.
14. Whitaker M, Elliott J, Chadeau-Hyam M, *et al.* Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508,707 people. Medrxiv. 2021; 13(6): 1957-1958.

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15. Bassatne A, Basbous M, Chakhtoura M, *et al.* The link between COVID-19 and VItamin D (VIVID): A systematic review and meta-analysis. Metabolism. 2021; 119(1):154753-154768.
16. Townsend L, Dyer AH, McCluskey P, *et al.* Investigating the relationship between vitamin D and persistent symptoms following SARS-CoV-2 infection. Nutrients. 2021; 13(7):2430-2441.
17. Fernández-de-Las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, *et al.* Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: A systematic review and meta-analysis. European journal of internal medicine. 2021; 92(2): 55-70.
18. Daneshkhah A, Agrawal V, Eshein A, *et al.* Evidence for possible association of vitamin D status with cytokine storm and unregulated inflammation in COVID-19 patients. Aging Clinical and Experimental Research. 2020; 32(1):2141-2158.
19. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infectious diseases. 2021; 53(10):737-754.
20. Pavli A, Theodoridou M, Maltezou HC. Post-COVID syndrome: Incidence, clinical spectrum, and challenges for primary healthcare professionals. Archives of medical research. 2021; 52(6): 575-581.
21. Elgendy SO, Elgendy MO, El-Gendy AO, *et al.* Health Care Workers' Awareness about the Post-COVID Syndrome and Different Types of COVID-19 Vaccines in Egypt. NeuroQuantology. 2020; 20(11): 3830-3839.
22. Gönen MS, Alaylıoğlu M, Durcan E, *et al.* Rapid and effective vitamin D supplementation may present better clinical outcomes in COVID-19 (SARS-CoV-2) patients by altering serum INOS1, IL1B, IFNg, cathelicidin-LL37, and ICAM1. Nutrients. 2021; 13(11): 4047-4066.
23. Castillo ME, Costa LM, Barrios JM, *et al.* 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. 2020; 203(1): 105751-105756.
24. Caballero-García A, Pérez-Valdecantos D, Guallar P, *et al.* Effect of vitamin D supplementation on muscle status in old patients recovering from COVID-19 infection. Medicina. 2021; 57(10): 1079-1087.

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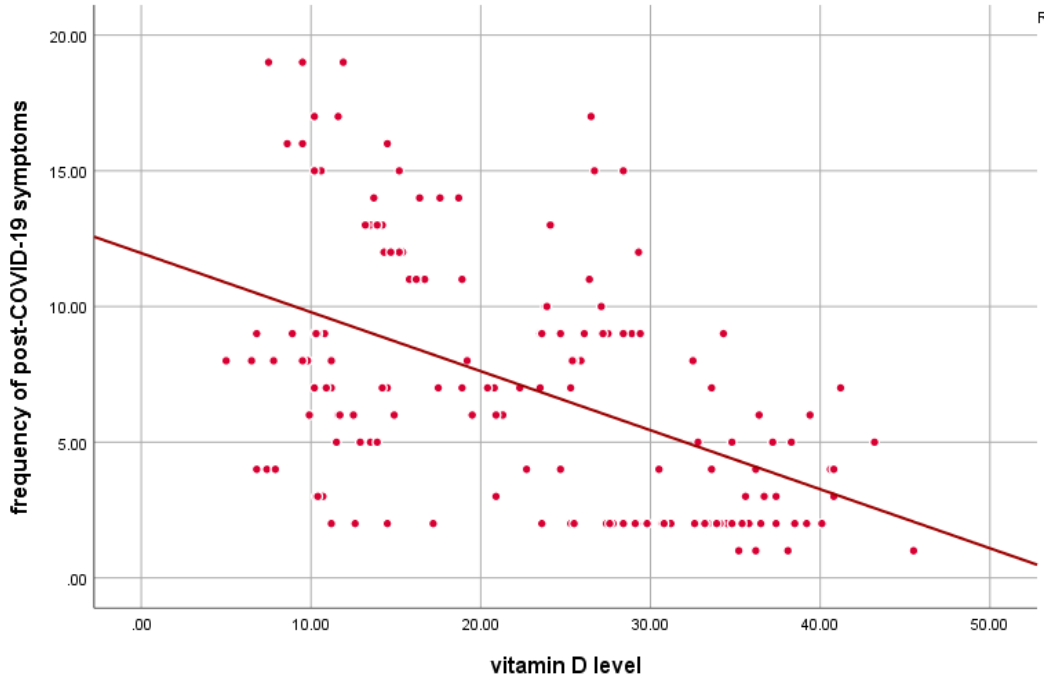
Table (1): Socio-demographic characteristics of post-COVID-19 participants

Parameter	Number 111	Frequency 100 %
Age		
• Mean ± SD	35.36±6.73	
• Min- Max	22-55	
Gender		
• Male	40	36.1
• Female	71	63.9
BMI		
• < 30 kg/m^2	93	83.8
• ≥ 30 kg/m^2	16	16.2
Smoking		
• No smoking	86	77.5
• Passive smoking	25	22.5
Pre-existing comorbidities		
• No or 1 comorbidity	73	65.8
• ≥ 2 comorbidities	38	34.2
Socioeconomic status (SES)		
• Middle	28	25.2
• High	83	74.8
Persistent post-COVID-19 symptoms:		
• Less than 3 symptoms	27	24.3
• 3 or more symptoms	84	75.7



R= -0.505 P-value= < 0.001

Figure (1): Correlation coefficient analysis of vitamin D levels and the frequency of persistent post-COVID-19 symptoms.

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Table (2): Comparison between intervention and placebo groups regarding post-intervention cardio-respiratory & neuropsychiatric symptoms

Parameter	Intervention group(N=55)	Placebo group (N=56)	Test of significance (U)	P-value
	Mean± SD			
Cardio-respiratory symptoms				
Dyspnea	1.2±0.4	1.1±0.1	1.77	0.077
Cough	1.4±0.8	3.0±1.9	4.12	<0.001**
Palpitation	1.5±1.0	2.4±2.0	2.36	0.019*
Chest pain	1.0±0.2	1.5±1.1	3.09	0.003*
Neuropsychiatric symptoms				
Fatigue	2.7±1.4	4.6±2.0	4.98	<0.001**
Sleep disturbance	1.7±0.8	4.1±2.3	5.19	<0.001**
Lack of concentration	2.6±6.7	3.9±2.0	4.59	<0.001**
Poor memory	1.7±0.8	3.6±2.3	4.79	<0.001**
Depressed mood	2.0±1.9	2.1±1.6	1.13	0.257
Headache	1.6±0.8	3.5±2.2	4.58	<0.001**
Anxiety	2.6±1.8	2.4±1.7	0.34	0.736
Anosmia	3.2±2.3	1.9±1.5	3.53	<0.001**
Loss of taste	3.0±2.1	1.9±1.7	3.26	0.001*
Vertigo	2.7±2.0	2.3±1.7	1.31	0.192
Tinnitus	2.4±2.0	2.0±1.6	0.61	0.543

SD: Standard deviation **U:** Mann-Whitney test

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Table (3): Comparison between intervention and placebo groups regarding post-intervention gastrointestinal, musculoskeletal, and general symptoms

Parameter	Intervention group(N=55)	Placebo group (N=56)	Test of significance (U)	P-value
	Mean± SD			
Gastrointestinal symptoms				
Loss of appetite	2.6±2.2	1.7±1.7	2.18	**0.029***
Diarrhea	1.5±1.0	1.1±0.6	2.95	**0.003***
Abdominal pain	1.4±0.9	1.2±0.6	0.71	0.480
Nausea/vomiting	1.2±0.6	1.1±0.3	0.98	0.325
Dysphagia	1.8±1.9	1.5±1.2	0.43	0.666
Musculoskeletal symptoms				
Myalgia	1.9±1.1	3.7±2.2	4.74	**<0.001****
Arthralgia	2.0±1.5	3.6±2.3	3.67	**<0.001****
Tingling sensation	1.4±0.8	2.0±1.6	1.44	0.149
General symptoms				
Sore throat	1.3±0.8	1.7±1.2	1.93	0.054
Lost weight (>3kg)	1.3±0.9	1.5±1.6	0.51	0.607
Skin rash\hair loss	1.2±0.4	2.3±1.6	3.71	**<0.001****
Menstrual cycle irregular	1.3±0.8	1.4±1.1	0.311	0.756

SD: Standard deviation **U:** Mann-Whitney test

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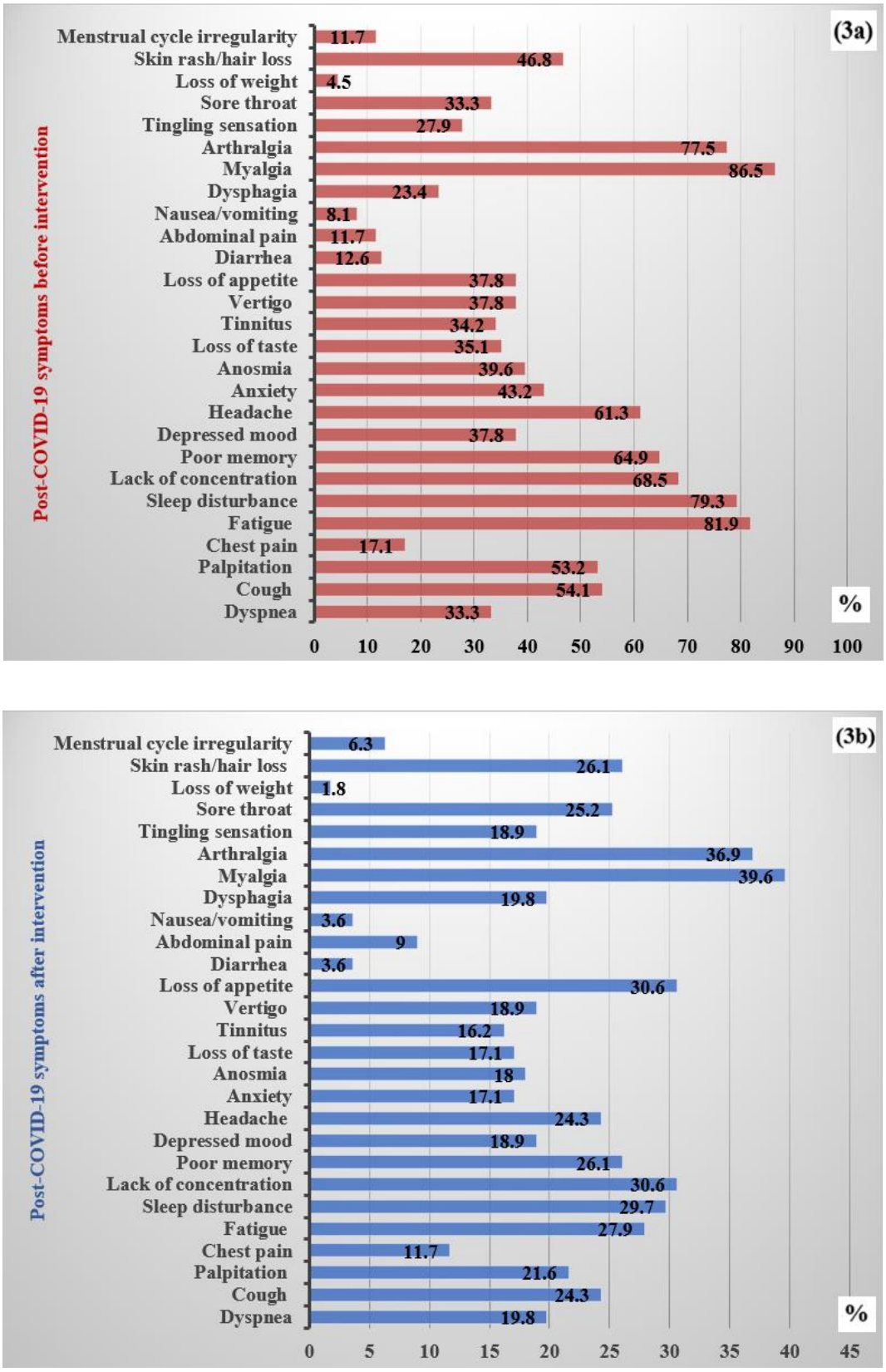

Figure (2): Comparative analysis of post-COVID-19 symptom severity pre-intervention (3a) and post-intervention (3b) in the studied cases

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الملخص العربي

تأثير فيتامين د على الأعراض المختلفة بعد الإصابة بعدوى الكوفيد-١٩: دراسة تداخلية

رفيدة محمد السقا - هالة محمد شاهين - نجوى نشأت حجازي- آية مصطفى بركات

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الخلفية: أعراض متلازمة ما بعد كوفيد-١٩ تحتوى على مجموعة واسعة من الأعراض. فيتامين (د)، هو أحد الفيتامينات المعروفة بخصائصها المناعية، و لها دور في الحد من الالتهابات الفيروسية ومضاعفاتها. **الأهداف:** تقييم تأثير العلاج بفيتامين (د) على تحسين أعراض متلازمة ما بعد الكوفيد-١٩. **طرق البحث:** تم إجراء دراسة سريرية تدخلية على ١١١ مريضًا في مرحلة ما بعد كوفيد-١٩. تم اختيارهم من العيادة الخارجية لمتابعة متلازمة أعراض ما بعد كوفيد-١٩ بمستشفى جامعة المنوفية في الفترة ما بين أكتوبر ٢٠٢١ ويونيو ٢٠٢٢. تم جمع البيانات الأساسية والتاريخ الطبي ثم قياس مستويات فيتامين (د) في الدم لدى جميع المرضى. بعد ذلك تم تقسيمهم عشوائيًا إلى مجموعتين: واحدة تتلقى فيتامين (د) عن طريق الفم يوميًا (٢٠٠٠ وحدة دولية) لمدة شهرين، والأخرى تتلقى أقراص لا تحتوى على أي مادة فعالة. تمت متابعة المجموعتين لمدة شهرين من العلاج. **النتائج :** من بين ١١١ فردًا يعانون من نقص مستويات فيتامين (د)، كان هناك انتشار أعلى بكثير لأعراض متلازمة ما بعد كوفيد-١٩. لوحظ وجود علاقة عكسية بين تعدد أعراض متلازمة ما بعد كوفيد-١٩ ومستويات فيتامين (د). بعد تدخل لمدة شهرين باستخدام فيتامين (د)، مقارنة بالعلاج الوهمي، كان هناك تحسن كبير في العديد من أعراض متلازمة ما بعد العدوى بكوفيد-١٩ مثل اعراض الجهاز التنفسي و الأعراض العصبية. **الإستنتاج:** هناك علاقة كبيرة بين نقص فيتامين(د) واستمرار أعراض متلازمة ما بعد الكوفيد-١٩، و لفيتامين (د) دور كبير في تحسين هذه الأعراض. **التوصيات:** تدعو الدراسة إلى القياس الروتيني لمستوي فيتامين-د لدى المرضى الذين تظهر عليهم أعراض متلازمة ما بعد الكوفيد-١٩، مع توصية بتناول فيتامين (د) في حالات نقصه.

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