The effect of Vitamin D Supplementation post Covid-19 infection and related outcomes: a systematic review and meta-analysis

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Abstract

Introduction

Vitamin D is widely recognized for its essential role in bone metabolism; however, its potential implications extend far beyond skeletal health. Recent research has highlighted the broader functions of vitamin D, particularly through its interaction with the vitamin D receptor (VDR), a ligand-dependent transcription regulator. This receptor, expressed by nearly all nucleated human cells, influences the expression of approximately 3% of the human genome, impacting a diverse array of physiological cellular processes via gene transcription. Numerous studies have explored the extra-skeletal roles of vitamin D, including its involvement in muscle metabolism, cancer prevention, diabetes prevention, cardiovascular function, and immune response. The onset of the SARS-CoV-2 pandemic has prompted further investigation into the potential role of vitamin D in infectious disease management.

Objectives

This meta-analysis aims to evaluate whether vitamin D can serve as a protective agent in patients with SARS-CoV-2 infection, focusing on its therapeutic role rather than a prophylactic one.

Materials and Methods

This systematic review and meta-analysis were registered on the PROSPERO database (CRD42023469826) and conducted following the PRISMA 2020 guidelines [1]. A comprehensive search was performed on PubMed/Medline, Scopus, Cochrane, and Google Scholar databases using a combination of keywords related to COVID-19 and vitamin D. Inclusion criteria included articles with relevant quantitative details on the relationship between vitamin D supplementation post-COVID-19 infection and outcomes, specifically RCTs, prospective studies, or retrospective studies. Exclusion criteria involved studies not directly pertinent to the query, lacking sufficient information, or not meeting the PICOS criteria. Data extraction and quality assessment were performed independently by two researchers, with meta-analysis conducted using STATA SE18. Statistical heterogeneity was assessed using I^2 statistics and the Heterogeneity χ^2 test, with significant heterogeneity leading to the use of a random-effects model.

Results

Mortality: The meta-analysis of 20 RCTs showed a non-significant trend towards reduced mortality with vitamin D supplementation (OR = 0.78, 95% CI: 0.60-1.03, $p = 0.08$). Subgroup analyses indicated significant mortality reduction during the early pandemic (OR = 0.17, 95% CI: 0.04-0.75) and in severe cases (OR = 0.50, 95% CI: 0.31-0.82), with older patients (≥65 years) also benefiting significantly (OR = 0.58, 95% CI: 0.39-0.87, $p = 0.01$). Analytical studies demonstrated a significant reduction in mortality risk (OR = 0.45, 95% CI: 0.24-0.86, $p = 0.02$), with a protective effect noted for general ward patients (OR = 0.41, 95% CI: 0.19-0.90). However, high heterogeneity ($I^2 = 66.96\%$) was observed in analytical studies.

ICU Admission: Vitamin D supplementation significantly reduced ICU admission risk by 44% in RCTs (OR = 0.56, 95% CI: 0.40-0.80, $p < 0.001$), with more pronounced effects in older adults (OR = 0.43, 95% CI: 0.26-

0.73) and high doses of vitamin D (OR = 0.38, 95% CI: 0.20-0.70). Analytical studies indicated a 65% reduction in ICU admission odds (OR = 0.35, 95% CI: 0.18-0.66, $p < 0.001$), with moderate heterogeneity ($I^2 = 54.70\%$).

Intubation: RCTs revealed a significant reduction in intubation rates (OR = 0.49, 95% CI: 0.27-0.88, $p = 0.02$) with low to moderate heterogeneity ($I^2 = 36.94\%$). Analytical studies showed a non-significant trend towards reduced intubation rates (OR = 0.65, 95% CI: 0.39-1.08, $p = 0.09$), with no heterogeneity ($I^2 = 0.00\%$).

Length of Stay: RCTs indicated a non-significant reduction in hospital length of stay (mean difference = -0.65 days, 95% CI: -1.38 to 0.08, $p = 0.08$) with substantial heterogeneity ($I^2 = 76.64\%$). Analytical studies showed a non-significant reduction in ICU length of stay (mean difference = -1.99 days, 95% CI: -6.89 to 2.92, $p = 0.43$), with substantial heterogeneity ($I^2 = 64.88\%$).

Conclusion

This comparative analysis of RCTs and analytical studies on vitamin D supplementation in SARS-CoV-2 patients highlights the potential benefits of vitamin D in reducing mortality, ICU admissions, and intubation rates. RCTs tend to show more consistent results with lower heterogeneity compared to analytical studies. While analytical studies indicate significant effects, particularly for mortality and ICU admissions, the high heterogeneity suggests the need for further investigation to clarify these findings. Both types of studies show non-significant trends towards reduced hospital length of stay, with substantial variability across studies. These findings underscore the importance of considering study design and patient characteristics in evaluating the role of vitamin D supplementation in COVID-19 management.

References

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