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## Diabetes &amp; Metabolic Syndrome: Clinical Research &amp; Reviews

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Letter to the Editor

## Does Vitamin D have a role to play in Covid-19 in the dexamethasone era?

*To The Editor:*

We read with interest the review and meta-analysis of the role of vitamin D in Covid-19 by Rawat et al. [1] and agree that studies to date are such, due to heterogeneity and sample size, that firm conclusions cannot be drawn.

Nevertheless, we would like to share our experience. We initially assessed any relationship between vitamin D deficiency and Covid-19 severity in hospitalised adults during the first wave of the pandemic in the UK and demonstrated that, during active infection, vitamin D deplete patients were more likely to develop cytokine storm and require ventilatory support [2].

Dexamethasone should be considered standard of care for patients with Covid-19 pneumonitis requiring respiratory support and the RECOVERY trial [3] demonstrated a reduction in all-cause mortality after 28 days. Considering these data, we explored the impact of dexamethasone therapy on vitamin D deficiency and Covid-19 severity [4].

Our two cohorts consisted of acutely hospitalised patients between March and April (“no dexamethasone”) and between September and December 2020 (“dexamethasone”). These were divided into vitamin D deficient (25-OH-D  $\leq$ 30nmol/L) and replete subgroups. No mortality difference was identified between cohorts and subgroups. The “no dexamethasone” cohort vitamin D deplete subgroup recorded significantly higher D-Dimer levels ( $p = 0.0309$ ), CRP ( $p = 0.0055$ ) and ventilatory support requirement ( $p = 0.007$ ) compared to the replete subgroup. Among the vitamin D deplete subgroup there was elevation of other markers of cytokine release, without statistical significance. In the “dexamethasone” cohort, there was no association between vitamin D deficiency and cytokine storm or ventilatory requirement. Our data suggest that dexamethasone mitigates adverse effects of vitamin D deficiency.

Corticosteroids modulate important components of the inflammatory and immune response seen in cytokine storm and this may explain why dexamethasone treatment seemingly negates effects of vitamin D deficiency. The diverse immuno-physiological actions of 1,25(OH)<sub>2</sub>D<sub>3</sub> are mediated by an intracellular vitamin D receptor (VDR) [5,6]. Both Vitamin D and dexamethasone share many VDR pathways [7], and based on these shared VDR attributes, it is reasonable to assume an interplay between vitamin D and

dexamethasone through related immunological mechanisms [8].

Notably, validation of dexamethasone therapy in the RECOVERY trial, render it unethical to conduct studies exploring vitamin D status in Covid-19 without dexamethasone. That being said, vitamin D is a simple intervention with undisputed health benefits, and vitamin D may still have a role to play. Further research might focus on Vitamin D supplementation in the community and prevention of hospitalisation from Covid-19.

**Declaration of competing interest**

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in the manuscript: **Does Vitamin D have a role to play in Covid-19 in the dexamethasone era?** Submitted to Diabetes and Metabolic Syndrome: Clinical Research and Reviews.

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