

## Review Article

# Possible role of vitamin D supplementation in coronavirus disease 2019

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### ABSTRACT

Vitamin D deficiency (VDD) is presumed to play a role in several infective and non-infective conditions such as acute respiratory infections, tuberculosis, diabetes, hypertension, stroke etc. Most of the respiratory viral infections occur during winter season when the vitamin D levels in most individuals are generally low. The current pandemic of coronavirus disease 2019 (COVID-19) which began during winter season similar to the previous epidemics due to coronaviruses, has again stirred a debate on the role of VDD in the initiation and spread of the pandemic. The data on vitamin D status in patients with COVID-19 is however lacking. Different vitamin D supplementation strategies have recently been suggested as part of several countermeasures aimed at reducing the impact of COVID-19 pandemic. This brief narrative review discusses the evidence for the link between VDD and COVID-19 and the approaches suggested for vitamin D supplementation.

**Keywords:** Coronavirus disease 2019, COVID-19, Vitamin D deficiency, Treatment, Vitamin D supplementation, Children

### BACKGROUND

The pandemic of coronavirus disease 2019 (COVID-19), probably the second most devastating in human history after the 1918 Spanish flu, has thrown life out of gear. The world's top, considered almost invincible, healthcare systems are facing ethical dilemmas in allocation of resources to the COVID-19 affected individuals.<sup>1</sup> There is no known prevention or cure of COVID-19, as the biomedical fraternity is frenetically trying to find one. A huge number of clinical trials to study the potential therapies for COVID-19 are being launched quickly in several countries in the midst of the pandemic underlying the need and competence to produce high-quality evidence.<sup>2</sup> The World Health Organisation has desperately announced studying even the unregistered and unproven therapies for COVID-19.<sup>3</sup> In such circumstances, the recent reports on the link between vitamin D deficiency (VDD) and COVID-19, and especially the

recommendations to improve the vitamin D status of population as well as the COVID-19 affected individuals, offer reassurance.<sup>4-6</sup> A report from Italy suggests treating VDD promptly with cholecalciferol in patients requiring hospitalisation.<sup>4</sup> Another report from Ireland recommends urgent vitamin D supplementation to older adults, hospital inpatients, nursing home residents and vulnerable groups such as those with diabetes mellitus, immunocompromised, vegetarians, obese, and healthcare workers with doses of 20-50 µg/day (800-2000 IU/day) of vitamin D.<sup>5</sup> It also recommends the supplementation advice to be quickly extended to the general adult population as well.<sup>5</sup> A recently published detailed review has suggested a population based strategy of vitamin D supplementation as one of the several countermeasures for the rampaging COVID-19 pandemic.<sup>6</sup> Curiously however, the recommended doses of vitamin D to be used in healthy individuals as well as those affected with COVID-19 in all these reports are quite varied.<sup>4-6</sup> Secondly, considerations

and recommendations for vitamin D supplementation in children during the pandemic are lacking probably because COVID-19 appears to have a mild course in children except in those with comorbidities.<sup>7,8</sup> A recent editorial suggests only ensuring baseline vitamin D sufficiency and cautions against using acute large doses of vitamin D in children.<sup>9</sup> A clear message about how and how much vitamin D is to be supplemented, is essential for the healthcare planners as well as professionals, who are currently fighting the pandemic crisis.

### WHAT IS THE NEED FOR VITAMIN D SUPPLEMENTATION?

Vitamin D is presumed to play a role in the prevention and recovery from infections by enhancing several immunoprotective processes in humans.<sup>6,10</sup> In autoimmune conditions such as type 1 diabetes, VDD is considered to be one of the several environmental triggers for the initiation and/or continuation of autoimmune processes in genetically predisposed individuals.<sup>11,12</sup> A similar role of VDD in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is yet to be studied. However, VDD could be one of the several host factors that contribute to create an optimal environment for virus replication, by either altering the host gene expression or by counteracting the host's antiviral defences.<sup>13</sup> Experience during the previous coronavirus epidemics did suggest the presence of host genetic susceptibility loci and differences in immune and inflammatory responses that affected the outcome of infection.<sup>13</sup> There is a possibility of a genetic predisposition to COVID-19 and/or to severe illness from COVID-19.<sup>14</sup> Data on vitamin D status of COVID-19 patients and its correlation with disease morbidity and mortality, is therefore, eagerly awaited. The initiation of several clinical trials on vitamin D supplementation in COVID-19 patients and their attending healthcare workers is therefore understandable.<sup>15</sup>

### WHAT IS THE RIGHT DOSE OF VITAMIN D SUPPLEMENTATION?

Grant WB et al rightly emphasized on the importance of rapidly raising the serum 25-hydroxyvitamin D (25(OH)D) concentrations to optimal levels of 40-60 ng/mL (100–150 nmol/L) by oral vitamin D intake.<sup>6</sup> Such high serum (25(OH)D) concentrations are required for vitamin D to exert immunoprotective as well as immunomodulatory effects.<sup>6,10,12</sup> During pandemic times, the usual measures such as modest sun exposure, food fortification and consumption of vitamin D rich foods cannot be relied upon to achieve desired serum 25(OH)D concentrations.<sup>16,17</sup> Therefore, the recommended vitamin D intakes of 10000 IU/day or 60,000 IU/week for about 4 weeks and then decreasing to 5000 IU/day are required to achieve optimal serum 25(OH)D concentrations. Loading doses of 200,000–300,000 IU at hospitalisation also appear necessary as serum 25(OH)D concentrations are expected to decrease during hospitalisation.<sup>6,18</sup> An appropriate vitamin D supplementation strategy in children could be using approximately half of the adult

doses with similarly reduced maintenance and loading doses. The upper tolerable limit of vitamin D intake in children is 4000 IU per day.<sup>19</sup> Vitamin D doses of upto 7000 IU per day have been shown to be well tolerated and safe over a 12-month duration of supplementation in children.<sup>20</sup> In our own experience, a daily cholecalciferol dose of 3000 IU could sustain serum 25(OH)D concentration of >30 ng/mL in 60% children only; 40% still remained vitamin D insufficient.<sup>21</sup> In addition, consideration has to be given for children belonging to different ethnicities and their ability to raise serum 25(OH)D concentrations in response to supplementation.<sup>22</sup> Children with associated conditions that interfere in vitamin D production from skin may require even higher doses.<sup>23,24</sup>

### INDIVIDUAL OR COMMUNITY BASED INTERVENTION?

While it is essential to raise and maintain serum 25(OH)D concentrations by individuals for their personal immunoprotection, the pandemic related vitamin D supplementation requires a community based intervention. The hypothesis proposed by Grant WB et al that VDD may be a contributory factor for initiation, spread, morbidity and mortality of COVID-19, appears quite plausible. After all, it cannot be without reason that almost all previous epidemics due to viruses began during winter seasons when 25(OH)D levels in the population are expected to be low.<sup>6</sup> Therefore, vitamin D supplementation is an intervention with a potential to at least slow the spread and impact of COVID-19 pandemic. It is relatively cheap and without significant adverse effects in comparison to the currently employed mainly experimental therapies in hospitalised COVID-19 patients.<sup>2</sup> The suggested approach for vitamin D supplementation is community based (and not only hospital based individual intervention) campaign aimed at making at least half of the population achieve optimal vitamin D status.<sup>6</sup> National government and medical professional bodies need to play a major role to accomplish this herculean task.

### CONCLUSION

Vitamin D sufficiency at the individual and community level may have a protective role against the SARS-CoV-2 infection, and should preferably be achieved through vitamin D supplementation to at least half of the general population during the COVID-19 pandemic.

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