ISSN: 2230-9926

*Available online at http://www.journalijdr.com*

IJDR

*International Journal of Development Research*
*Vol. 10, Issue, 08, pp. xxxxxxxxxx, August, 2020*
https://doi.org/10.37118/ijdr.xxxxx.08.2020

RESEARCH ARTICLE OPEN ACCESS

# VITAMIN D. COVID-19 RISK PREVENTION RECOMMENDATIONS: A REVIEW

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**ARTICLE INFO**

***Article History:***
Received xxxxxx
Received in revised form
xxxxxx
Accepted xxxxxxxxx
Published online xxxxxxxxxxxx xxx

***Key Words:***

Aprendizagem colaborativa.
Interação. Autonomia. Participação.

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**ABSTRACT**

The pandemic caused by the type 2 coronavirus that started in late 2019 in Wuhan, China, has affected the world with devastating consequences for the health systems and the economy of different countries affected. The high transmissibility of the virus contributes to the high rates of cases and deaths by Covid-19. This disease presents with different clinical forms ranging from cases with few symptoms to others of high severity with severe acute respiratory syndrome (SARS) responsible for most deaths. In the lung, the respiratory epithelium is the first line of defense against the penetration of inhaled pathogens and vitamin D is essential for the innate and adaptive immunity system. Most immune cells including B lymphocytes, T lymphocytes, monocytes, macrophages and dendritic cells express vitamin D (VDR) receptors.Therefore, in the current context of this evolving pandemic with high rates of cases and deaths and the prospect of progression, it would be pertinent to apply preventive measures aimed at the organic defenses of each individual with their particularities regarding age and lifestyle and comorbidities.

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**Citation:** ***Maria da Conceição N. Pinheiro; Dirce Nascimento Pinheiro1 Murilo Eduardo Soares Ribeiro; Ademir Ferreira da Silva Júnior, Antônio Vivaldo Pantoja and José Aglair Barbosa de Freitas Junior.*** **2020** "Vitamin D. Covid-19 risk prevention recommendations: a review", *International Journal of Development Research*, 10, (08), xxxxxxxxxxxxxx.

## INTRODUCTION

The pandemic caused by the type 2 coronavirus that started in late 2019 in Wuhan, China, has affected the world with devastating consequences for the health systems and the economy of different countries affected. The high transmissibility of the virus contributes to the high rates of cases and deaths by Covid-19. This disease presents with different clinical forms ranging from cases with few symptoms to others of high severity with severe acute respiratory syndrome (SARS) responsible for most deaths (Hu *et al*, 2020). In the world, until July 10, 2020, 12,615,749 cases and 562,017 deaths were recorded by covid-19, attributing a variable mortality rate by continent, countries and regions (www.worldometers.info/coronavirus/). In Brazil, 1,804,338 cases and 70,524 deaths (332 deaths / 1 million inhabitants) were recorded up to these data, with different distribution by states and cities, with no apparent connection with climate, temperature and temperature. The states in the northern region have been affected like the states in the northeast region. And, in most of the countries observed, there was an important involvement in young people, although the prevalence is in the elderly (MS, 2020). Among the factors that can explain the high rates of cases and deaths by Covid 19 in the world, the immune defense mechanisms of individuals and populations exposed to coronavirus-2 stand out. In this association, there is evidence of the importance of vitamin D concentrations in immune protection against acute respiratory infections. In order to identify ideal blood levels of vitamin D for respiratory immune protection, as well as adequate and safe supplementation values for the prevention of covid-19, a brief review of the recent literature was carried out using the terms: vitamin D and Covid, vitamin D and viral infections, supplementation and vitamin D.

**Vitamin D and immunity:** In the lung, the respiratory epithelium is the first line of defense against the penetration of inhaled pathogens. The rapid and non-specific recognition of pathogens is developed by innate immunity. Vitamin D increases innate cellular immunity through the induction of antimicrobial peptides, including catelecidin LL-37 and defensin Beta-2, increasing phagocytosis and the death of these pathogens. The adaptive immune response is related to acquired immunity and involves the ability of T lymphocytes and B lymphocytes to produce cytokines and immunoglobulins respectively (Hansdottir *et al*, 2008). Vitamin D is essential for the innate and adaptive immunity system. Most immune cells including B lymphocytes, T lymphocytes, monocytes, macrophages and dendritic cells express vitamin D (VDR) receptors (Sassi, Tamone and D´Amélio, 2018). In addition, these cells show an active metabolism converting the inactive form (25OHvit D3) to the active form (1.25 (OH) 2D3) (Hansdottir *et al*, 2008). In Covid -19, when the virus goes beyond the first defense barriers of the respiratory system, pro-inflammatory cytokines, including interleukin (IL) -1β and IL-6, are released promoting inflammatory reaction in the lungs and systemic manifestations such as fever (Contri *et al*, 2020). The complications resulting from these viral infections are often due to the hyperinduction of the production of these pro-inflammatory cytokines also known as cytokine storm (Li and Yang, 2016). Associated with the inflammatory reaction, there may also be activation of coagulation reactions with the formation of microthrombi in the pulmonary circulation, which can progress to severe respiratory distress syndrome (SARS), which is responsible for most deaths by Covid-19 (Xiang-Hua, Y. *et al*. (2010). The access of the virus to the respiratory tract epithelial cell is associated with its S protein that activates and alters the angiotensin-converting enzyme 2 (ACE-2). The regulatory function of ACE-2 in the production of angiotensin is impaired by altering the renin-angiotensin-aldosterone system. This mechanism also appears to be involved in the pathogenesis of respiratory and cardiovascular complications in Covid-19 (Wevers and Van der Hoek, 2010).

**Epidemiological and clinical studies of Covid and vitamin D association:** There is epidemiological, clinical and experimental evidence of the role of vitamin D in preventing, treating and reducing mortality from acute viral infectious diseases, such as influenza and Covid (Sabetta et.al, 2010; Grant *et al*, 2020; Daneshkhah *et al*, 2020). This role appears to be related to vitamin D-dependent innate immunity. Low levels of vitamin D are associated with worsening Covid-19 outcome (Speeckaert M.M. and Delanghe J.R; 2020). The importance of vitamin D has been assessed in the current SARs-CoV 2 epidemic in different studies in Europe (Germany, Switzerland, France, the United Kingdom, Italy and Spain) and in Asia (China, Iran, South Korea) using average concentrations 25-hydroxyvitamin D. Italy, Spain and France presented the lowest concentrations in relation to the limit established for severe deficiency. Italy registered an average of 19.9ng / ml and Spain with 22.5ng / ml. These two countries also had the highest mortality rates from Covid-19 (Daneshkhah *et al*, 2020). Another study involving patients with Covid-19 showed that lethality rates were associated with age and with serum concentrations of 25 (OH) vit D reduced as age increased (Hui-Jin Hu *et al*, 2016; Novel, 2020). Chen *et al* (2007) had already observed that age, skin color and diet are factors that influence the cutaneous synthesis of vitamin D. The effects of age, in addition to gender and seasonal variation on serum 25-OH- vitamin D have been demonstrated by Hui-Jin Hu *et al*, (2016). Several systematic review studies have shown the positive impact of vitamin D supplementation on human health, especially on bone health and the prevention of respiratory infectious diseases (Vengeles&Ekwaru, 2014; Autier *et al*, 2017; Kimball, Mirhosseini&Holick, 2017 ; Zhou *et al*, 2019; Martineau *et al*, 2020). A meta-analysis study involving randomized, double-blind, placebo-controlled trials with vitamin D3 and D2 supplementation, demonstrated safety and protection against acute respiratory tract infections. For this meta-analysis, 25 articles were evaluated involving 10,933 patients with acute respiratory infections (Martineau *et al*, 2017). Zhou *et al* (2019) evaluated the effects of vitamin D supplementation on non-skeletal disorders through eight systematic review articles with meta-analysis involving adult patients and children and found that patients with community-acquired pneumonia (CAP) had concentrations of 25 -OH-vit D below 20ng / ml. Beside that, Vengeles&Ekware, 2014 admit that miscalculations in the recommended dose (RAD) for vitamin D supplementation can have serious clinical implications for public health in the prevention and treatment of bone and other vitamin D-dependent diseases.

The current recommended dose of 600 IU / day does not meet organic needs, especially in the elderly and in individuals where skin synthesis by sunlight is not viable. It also admits that the current reference doses do not meet the organic needs, especially for the elderly and individuals whose vitamin D synthesis is impaired and a review of the reference dose is recommended. Effects of vitamin D supplementation on non-skeletal disorders were analyzed through systematic review with meta-analysis and randomized screenings involving adults and children. The main finding of this review was that vitamin D supplementation should help to prevent infections of the upper respiratory tract and exacerbation of asthma (Autier *et al*, 2017). Kimball, Mirhosseini&Holick, (2017) characterized the effect of vitamin D supplementation at maximum doses of 15,000 IU / day in a program based on vitamin D status, calcium homeostasis, as well as on renal, liver and immune function. This study involved 3,882 individuals who were supplemented with doses ranging from 1,000-15,000 IU / day to achieve blood levels of 25-OH-vitamin D, at least 100nmol / L. The maximum concentration of 300nmol / L was achieved without changes in calcium homeostasis or signs of toxicity (hypercalcemia, hypercalciuria). To achieve doses greater than 100nmol / L in 25-OH-vitamin D serum, an intake of 6,000 IU / day is required for individuals with normal BMI, 7,000 IU for overweight individuals and 8,000 IU for obese individuals. Other authors also recommend supplementation of 20-50 µg / day (800-2,000 IU / day) of vitamin D to increase resistance to Covid-19 and this recommendation can be readily extended to the general adult population (Mc Cartney and Byrne, 2020).

In Brazil, despite the favorable latitude situation, there is evidence of vitamin D3 deficiency. Palmeira *et al* (2016) showed a high prevalence of low concentrations of 25-hydroxy vitamin D in the serum of residents in a tropical region in the Brazilian Amazon, with a total of 226 patients seen at a referral hospital for cardiovascular diseases in the region. Hypovitaminosis D, in particular, vitamin D levels <30 nmol / L was associated with high rates of atherosclerotic block and predominance of multifactorial involvement. Another study involving the elderly, the authors observed a high prevalence of vitamin D deficiency and insufficiency in a geriatric population, which was more pronounced in the

institutionalized group, but also evident among community residents (Saraiva *et al*, 2007). Recently, the Brazilian Society of Endocrinology and Metabolism and the Brazilian Society of Clinical Pathology, in review of parameters, established, in 2017, the concentration of ≥30ng / mL of 25-OH-vitamin D as desirable for the population at risk of hypovitaminosis D, and defined reference values for 25-OH-vitamin D stratified according to age and individual characteristics: deficiency: <20ng / mL; levels suitable for the general population <65 years: 20-60ng / ml; ideal level: 30-60ng / mL; risk of intoxication:> 100ng / mL.

**Conclusions and recommendations**

The role of the innate immune system in the evolution of Covid -19 is notorious and the epidemiological, clinical and experimental evidence indicates the importance of vitamin D in strengthening this immunity. Therefore, in the current context of this evolving pandemic with high rates of cases and deaths and the prospect of progression, it would be pertinent to apply preventive measures aimed at the organic defenses of each individual with their particularities regarding age and lifestyle and comorbidities. Only public health sanitary practices (hand washing, wearing masks, reducing social contact) are not enough to contain the pandemic's progress. Control through vaccines is a medium and long-term expectation that the world looks forward to, but in the meantime, the use of other preventive measures based on scientific evidence to minimize the damage resulting from this pandemic can be a benign measure. The role of vitamin D in reducing the risk of acute respiratory infections is well known from epidemiological studies and clinical trials of supplementation. And, while new therapies and vaccines are not yet available, added to the need to maintain social isolation, with the impossibility for many of sun exposure, supplementation of vitamin D3 (cholecalciferol) can be an urgent, affordable and low-cost control measure. of the pandemic, especially to reduce lethality. The adoption of this practice in public health, safely, under medical control aiming to reach ideal levels based on evidence, a supplementation of 20-50µg / day are sufficient and safe. This measure can have a positive impact, mainly, in the reduction of severe forms and in the mortality associated with Covid-19.

## REFERENCES


Autier P, Mullie P, Macacu A, Dragomir M, Boniol M, Coppens K, Pizot C, Boniol M. Effect of vitamin D supplementation on non-skeletal disorders: a systematic review of meta-analyses and randomised trials. Lancet Diabetes Endocrinol., v.5, p.986-1004, 2017. doi: 10.1016/S2213-8587(17)30357-1.

Brasil. Ministério da Saúde. Painel coronavírus no Brasil [acesso em 27 jun 2020]. Disponível em: https://covid. saude.gov.br/.

Chen T.C., Chimeh F., Lu Z., Mathieu J., Person, K.S., Zhang A., Kohn N., Martinello S., Berkowitz R., and Holick M.F. Factors that Influence the Cutaneous Synthesis and Dietary Sources of Vitamin D. Arch BiochemBiophys, v.460, n.2, p.213–217, 2007. doi:10.1016/ j.abb.2006.12.017.

Conti P, Ronconi G, Caraffa A, *et al*. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. J BiolRegulHomeost Agents., v.14, n.34(2),2020. doi: 10.23812/CONTI-E. [Epub ahead of print] COVID-19 CoronavirusPandemic.

Daneshkhah A., Eihein A., Subranmanian H., Roi H.K. and Backman V.The Role of Vitamin D in Suppressing Cytokine Storm in COVID-19 Patients and Associated Mortality. 2020. medRxiv preprint doi: https://doi.org/10.1101/2020.04.08.20058578.

Disponível <https://www.worldometers.info/coronavirus> acesso em 25.06.2020. doi:10.1038/cmi.2015.74.

Ferreira CE, Maeda S, Batista MC, Lazaretti-Castro M, Vasconcellos LS, Madeira M, *et al*. Consensus – reference ranges of vitamin D [25(OH)D] from the Brazilian medical societies. Brazilian Society of Clinical Pathology/Laboratory Medicine (SBPC/ML) and Brazilian Society of Endocrinology and Metabolism (SBEM). J BrasPatolMed Lab.; v.53(6), p.377-81, 2017.

Grant, W.B., Lahore H., McDonnell S.L., Baggerly C.A., French C.B., Aliano J.L., and BhattoaH.P.. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. Nutrients, v.12, p.988, 2020; doi:10.3390/nu12040988

Hansdottir S, Monick MM, Hinde SL, Lovan N, Look DC, Hunninghake GW. Respiratory epithelial cells convert inactive vitamin D to its active form: potential effects on host defense. J Immunol.; v.181,n.10,p.7090-7099,2008.

Hu Z.; Song C.; Xu C.; Jin G.; Chen Y.; Xu X.; Ma H.; Chen W.; Lin Y.; Zheng Y.; Wang J.; Hu Z.; Yi Y.; Shen H. Clinical Characteristics of 24 Asymptomatic Infections with COVID-19 Screened among Close Contacts in Nanjing, China. medRxiv preprint doi: https://doi.org/10.1101/2020.02.20.20025619.

Hui-Jin Yu, Min-Jung Kwon, Hee-Yeon Woo, and Hyosoon Park. Analysis of 25-Hydroxyvitamin D Status According to Age, Gender, and Seasonal Variation. Journal of Clinical Laboratory Analysis, v.30, p.905–911, 2016.

Kimball SM, Mirhosseini N, Holick MF. Evaluation of vitamin D3 intakes up to 15,000 international units/day and serum 25-hydroxyvitamin D concentrations up to 300 nmol/L on calcium metabolism in a community setting. Dermatoendocrinol.2017; 9:e1300213. doi: 10.1080/19381980.2017.1300213.

Liu Q, Zhou YH, Yang ZQ. The cytokine storm of severe influenza and development of immunomodulatory therapy. Cell MolImmunol., v.13(1),p.3–10, 2016.

Martineau A.R.*et al*. Vitamin D supplementation to prevent acute respiratory tract infections: Systematic review and meta-analysis of individual participant data. BMJ,356:i6583,2017. Doi: 10.1136/bmj.i6583.

McCartney D.M., Byrne D.G. Optimisation of Vitamin D Status for Enhanced Immuno-protection Against Covid-19. Ir Med J.; v.113; n.4; p58, 2020.

Novel, C.P.E.R.E. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing XueZaZhi, v.41,p.145–151, 2020.

Palmeira M.M.; Neves J.S., Ribeiro H.Y.U., Neto F.O.M.J., Rodrigues I.S. and Pinheiro M.C.N.Vitamin D: Emerging Risk Factor for Acute Myocardial Infarction, J Thrombo Cir, v.4, n.1;p. 4, 2018.

Sabetta JR, DePetrillo P, Cipriani RJ, Smardin J, Burns LA, Landry ML. Serum 25-hydroxyvitamin d and the incidence of acute viral respiratory tract infections in healthy adults. PLoS One 2010; 5: e11088.

Saraiva G.L., Cendoroglo M.S., Ramos I.R., Araújo L.M.Q., Vieira J.G.H., Maeda S.S., Borba V.Z.C, Kunii H., Hayashil. F., Lazaretti-Castro M. Arq Bras EndocrinolMetab; v.51/3, p.437-442, 2007.

Sassi F., Tamone C. and D' Amelio P. Vitamin D: Nutrient, hormone and immunomodulatory. Reviews Nutrients, v.10, n..1656, 2018. Doi: 10.3390/nu 10111656.

Speeckaert M.M and Delanghe J.R. Association between low vitamin D and COVID−19: don't forget the vitamin D binding protein. Aging Clinical and Experimental Research. https://doi.org/10.1007/s40520-020-01607-y

Veugelers, P.J. and Ekwaru, J.P., A Statistical Error in the Estimation of the Recommended Dietary Allowance for Vitamin D. Nutrients, v.6, p.4472–4475, 2014; doi:10.3390/nu6104472 *Nutrients.* 2015; 7:1688–1690. doi: 10.3390/nu7031688.

Wevers BA, Van der Hoek L. Renin-angiotensin system in human coronaviruspathogenesis. Future Virol; v.5, p.145–61, 2010.

Xiang- Hua, Y. *et al*. Severe acute respiratory syndrome and venous thromboembolism in multiple organs. Am. J. Respir. Crit. Care Med., v.182, p.436–437, 2010.

Zhou YF, Luo BA, Qin LL. The association between vitamin D deficiency and community-acquired pneumonia: A meta-analysis of observational studies. Medicine (Baltimore). 2019; 98:e17252. doi: 10.1097/MD.0000000000017252.