Brief Report

Impact of COVID-19 pandemic on serum 25-hydroxyvitamin D levels in Brazilian patients

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Abstract: Governmental actions and public health recommendations during the coronavirus disease 2019 (COVID-19) pandemic resulted in several restrictions on daily living, including social distancing. The impact of these long-term restrictions on health behaviors and lifestyles are unclear, but it could be related to vitamin D (VitD) deficiency. This study aimed to compare VitD levels in patients in pre-pandemic (PP) period and during the most important isolation period in pandemic (DP). We investigated 363,158 results of 25-hydroxyvitamin D (25OH-D) levels from individuals who underwent health checks. The data was obtained from medical records during 2018–2019 (PP); and those results obtained from 2020 to 2021 (DP). 25OH-D levels were measured using a chemiluminescent assay (Siemens®). R software was used to statistical analysis and P value <0.05 was considered significant. 25OH-D levels were compared also regarding age ranges (<18, 18–64 and ≥65 years old) and sex of the individuals. The men group presented higher 25OH-D levels than women only in PP period. During the PP period, individuals <18 years old also showed higher 25OH-D levels. All age groups presented lower 25OH-D levels in DP period, however, the greatest reduction was observed in the group <18 years old. VitD evaluation and supplementation should be considered for overall population submitted to home confinement and social distancing due to COVID-19.

Keywords: 25-hydroxyvitamin D (25OH-D); coronavirus disease 2019 (COVID-19); lockdown; social distancing

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Vitamin D (VitD) is a fat-soluble hormone synthesized principally under ultraviolet B radiation in the skin epithelium (1). The main circulating form of VitD, the 25-hydroxyvitamin D (25OH-D), is metabolized in the liver prior conversion in the kidney to its hormonal form (calcitrol), which regulates calcium and phosphate homeostasis (1). The expression of the VitD receptor (VDR) and VitD-metabolizing enzymes in almost all tissues suggest a widespread role of VitD for overall human health. Severe VitD deficiency is related to the increased risk of non-communicable, immune, and infectious diseases (2,3).

Meta-analyses about VitD suggest that its supplementation may reduce the incidence of cancer mortality, acute respiratory infections, as well as chronic obstructive pulmonary disease exacerbations and asthma. Besides, there is accumulating evidence suggesting potential benefits of VitD for the prevention and treatment of coronavirus disease 2019 (COVID-19) (4), although it is not completely clear. Therefore, its blood level should be regularly monitored by clinicians.

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Table 1 25OH-D levels (ng/mL) in PP and DP periods according to the age and sex

Group	PP period	DP period	P value
All	29.61±10.03	26.90±11.25	<0.001*
Gender			
Women	29.38±9.98	26.89±11.26	<0.001*
Men	30.35±10.14	26.91±11.22	<0.001*
P value	<0.001*	0.902	–
Age, years			
<18	31.14±10.24	24.16±9.52	<0.001*
18–64	28.81±9.78	26.09±11.12	<0.001*
≥65	30.77±10.30	29.01±11.46	<0.001*
P value			
P^1	<0.001*	<0.001*	–
P^2	<0.001*	<0.001*	–
P^3	<0.001*	<0.001*	–

Values presented as mean ± standard deviation. P^1: <18 *vs.* 18–64 groups; P^2: <18 *vs.* ≥65 group; P^3: 18–64 *vs.* ≥65 years old groups. *, significant: P<0.05. 25OH-D, 25-hydroxyvitamin D; PP, pre-pandemic; DP, during the most important period in pandemic.

Governmental actions and public health recommendations during the COVID-19 pandemic resulted in several restrictions on daily living, including isolation, home confinement, quarantine, lockdown and social distancing. Obviously, these measures were imperative to decline the dissemination of COVID-19, but the impact of these long-term restrictions on health behaviors and lifestyles are unclear until now. An international online survey, launched in April 2020, showed that food consumption and meal patterns (the type of food, number of main meals, eating out of control, snacks between meals) were unhealthier during this period (5). Consequently, the implementation of the measures to minimize the impacts of COVID-19 outbreak reduced outdoor activities and sun exposure, which could be related to VitD deficiency.

We aimed to compare VitD levels in Brazilian patients in 2018–2019 [pre-pandemic (PP) period] and 2020–2021 [during the most important period in pandemic (DP)], according to age and sex.

This study included 363,158 tests of 25OH-D levels from outpatients who underwent health checks at Lustosa Clinical Laboratory based in Minas Gerais, Brazil. The data was obtained from medical records during 2018–2019 (n=172,180 tests–PP); and those results obtained from 2020 to 2021 (n=190,978 tests–during DP). 25OH-D levels were measured using a chemiluminescent assay (Siemens®). R software was used to statistical analysis and P value <0.05 was considered significant. 25OH-D levels were compared also regarding age ranges (<18, 18–64 and ≥65 years old) and sex of the individuals. Ethical Committee exempted the study from the need for review, because it is only based on medical records search. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

We applied a clustering algorithm called SHapley Additive exPlanation (SHAP) in order to evaluate the 25OH-D values that have more probability to predict the period (PP or DP). SHAP is an effective machine learning model interpretation, whose effect of the variable was calculated by the distance from the original prediction (6). A mean of absolute distances for each individual was used to generate a graphic that shows the 25OH-D concentration according to period prediction. A negative distance was obtained if the individual 25OH-D value was in the PP, and a positive distance was obtained when the individual 25OH-D value was in the DP periods.

The 25OH-D levels PP and DP periods, as well as the comparison between sex and age classes, were showed in *Table 1*. The 25OH-D levels were lower in DP than PP periods for all populations, independently of sex and age (P<0.001). The men presented higher 25OH-D levels than

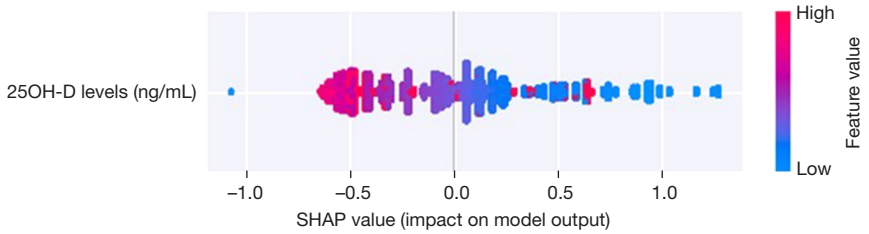

Figure 1 SHAP clustering algorithm showing the 25OH-D levels according to the pandemic period. Values below 0 on the X axis are related to pre-pandemic period and values above 0 are related to pandemic period. The red color indicates greater values of 25OH-D, and blue color specifies lower values of 25OH-D. 25OH-D, 25-hydroxyvitamin D; SHAP, SHapley Additive exPlanation.

women group only in PP period (P<0.001). In DP period, the 25OH-D levels between the sex were not different (P=0.902).

During the PP period, individuals <18 years old showed higher 25OH-D levels than other groups (18–64 and ≥65 years; P<0.001 for all). All age groups presented lower 25OH-D levels in DP period (P<0.001), however, the greatest reduction was observed in the group <18 years old (*Table 1*).

Considering that 30 ng/mL is the reference value for this test, men, <18 and ≥65 years old groups presented values above this concentration in PP period. However, in DP period, all the groups, independently of sex and age, presented VitD deficiency with mean values <30 ng/mL.

The SHAP shows that values below 0 on the X axis tend to be related to PP period and values above 0 tend to be related to DP period. The red color indicates greater values of 25OH-D, and blue color specifies lower values of 25OH-D. The SHAP algorithm showed that higher 25OH-D levels are more probable to be encountered during PP period, which corroborates our previous data (*Figure 1*).

Our results showed that 25OH-D levels DP period was lower than PP period between overall age and sex, which is in line with other studies that investigated these levels in children and adolescents in different populations (7-9). Changes in lifestyle caused by the COVID-19 pandemic, such as quarantine, home confinement and home office, decreased sunlight exposure and have influenced the 25 OH-D levels. Our data suggest a relationship between changes in society behavior and VitD levels after COVID-19 outbreak.

In PP period, 25OH-D levels in women were lower than men group, but during pandemic period, no difference was reported between the sexes. This finding suggests that men were more affected by the public health measures of distancing, probably due to reduced occupational sun exposure during the pandemic. People <18 years old also showed more evident 25OH-D reduction. Probably, this group executes most of their daily activities outside, which suffered greater impact due to lockdown.

Lippi *et al.* (10) did not observe 25OH-D values difference between 2,327 outpatients considering females and males, and observed a similar prevalence of mild and moderate 25OH-D deficiency between the sexes. A non-significant variation of 25OH-D values was also found by analysis throughout four age cohorts (<21, 21–40, 41–60 and >60 years old), in both genders. The percentage of subjects presenting mild and moderate 25OH-D deficiencies in the older group was comparable to that observed in the younger adult population (10). Hilger *et al.* found age-related 25OH-D differences only in the Asia/Pacific and Middle East/Africa regions, but sex-related differences were not observed in any region. However, the analyses suggested that newborns and institutionalized elderly seemed to be at a higher risk of exhibiting lower 25OH-D values (11). It is important to emphasize that Brazil is a tropical country with highest solar incidence, which explains that frequency of VitD deficiency could be different from other populations. Moreover, groups with greater daily sun exposure were the most affected by the home office during pandemic period.

Currently, VitD deficiency has been reported as a worldwide task, even before the COVID-19 pandemic. Consequently, VitD supplementation is encouraged specially to risk groups, as obese or elderly people (12,13). However, based on our evidence that 25OH-D levels have decreased due to public actions to reduce COVID-19 transmission, screening and supplementation should be considered for overall population submitted to home confinement or quarantine due to COVID-19. In agreement with this

hypothesis, our results showed that all the groups presented VitD deficiency in DP period.

Further studies are necessary in order to clarify whether VitD can restore the immune balance to prevent the hyper-inflammatory cytokine storm related to severity in COVID-19, besides controlling initial viral replication, reducing the survival of viruses, and reducing risk of inflammatory cytokine production, increasing angiotensin-converting enzyme 2 concentrations, and maintaining endothelial integrity (14,15). However, the benefits of VitD supplementation in the treatment of COVID-19 remain controversial and it needs to be definitively clarified whether a VitD supplementation can also be recommended for a subject vaccinated against COVID-19 (16,17). As far as we know, this is the first study that investigates, in a large population, 25OH-D levels according to the pandemic period, also considering the age and sex variable.

In conclusion, all sex and age groups presented deficiency and lower 25OH-D levels in DP period. Consequently, VitD supplementation should be evaluated for general populations submitted to public health measures, such as social distancing, due to COVID-19.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jlpm.amegroups.com/article/view/10.21037/jlpm-23-35/coif). KBG serves as an unpaid editorial board member of *Journal of Laboratory and Precision Medicine* from August 2023 to July 2025. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Ethical Committee exempted the study from the need for review because it is only based on medical reports search. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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