## **Short Report**

# Is COVID-19 lockdown associated with vitamin D deficiency?

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All vitamin D tests carried out for outpatients aged 18 years or older during the last 3 years at an Italian University Hospital was reviewed. The serum vitamin D concentrations measured since the Italian coronavirus diseases 2019 (COVID-19) lockdown to present did not significantly differ from the previous 2 years (78 vs. 77 nmol/l; P = 0.277), whilst the prevalence of vitamin D deficiency was found to be even marginally lower in 2020 (16.0% vs. 17.9%; P = 0.003). These results suggest that vitamin D deficiency in our province has not increased during the Italian COVID-19 outbreak or in correspondence with the nationwide lockdown.

#### Introduction

There is now unquestionable evidence that the ongoing coronavirus diseases 2019 (COVID-19) pandemic outbreak is causing immense consequences on population health, society and economy, by both causing a deadly form of infection and by persuading many national governments to establish strict policies that limit individual freedoms and movements, such as stay-at-home orders and/or lockdowns. Home segregation of large parts of the population not only may jeopardize care access, but would also be associated with detrimental biologic and metabolic consequences. Vitamin D, a fatsoluble hormone scarcely available from foods, is mostly generated through biological activation of its precursors into the biologically active form by sunlight exposure. Despite controversies still remain about the potential extra-skeletal effects of vitamin D, <sup>3</sup> several lines of evidence attest that it may have an essential role in helping the organism to provide a more effective defence against bacterial and viral infections. In particular, it has also been recently shown that COVID-19 patients with vitamin D deficiency may be at higher risk of developing severe or critical form of illness. 5,6 Therefore, this work was aimed at assessing as to whether the COVID-19 ongoing outbreak, along with the associated social restrictions, may have impacted the vitamin D status of the general population.

#### **Methods**

The Service of Laboratory Medicine of the general Hospital of Verona ( $\sim$ 1200-bed facility) provides routine and urgent laboratory diagnostics for the center of the town and for northern part of the province, thus serving a population of  $\sim$ 400 000 inhabitants. Routine laboratory diagnostics for outpatients has been exempted from national, regional and provincial mobility limitations even throughout the local COVID-19 lockdown period (i.e. between 10 March and 17 May 2020).

We performed an electronic search in our laboratory information system (LIS) aimed at retrieving all vitamin D tests carried out in outpatients aged 18 years or older during the last 3 years (i.e. from 11 December 2018 to 11 December 2020). The serum vitamin D [25(OH)D] concentration has been assayed throughout the study with the same Liaison instrumentation (DiaSorin, Saluggia, Italy).

The accuracy and reproducibility of test results was validated by regular internal quality control procedures and participation in External Quality Assessment Schemes. The inter-group differences of serum 25(OH)D concentrations were analysed with Mann–Whitney U and Pearson's  $\chi^2$  tests, when appropriate, using Analyse-it (Analyse-it Software Ltd, Leeds, UK). The study was performed in accordance with the Declaration of Helsinki, under the terms of relevant local legislation. Test results were downloaded from the LIS in fully anonymized format during systematic monitoring of laboratory activity as required for maintenance of ISO 15189:2012 accreditation, so that no patients' informed consent or Ethical Committee approval were necessary.

#### Results

The results of this analysis are summarized in table 1. The median serum 25(OH)D concentration was found to be slightly but not significantly higher comparing the period comprised between the first day of Italian lockdown (i.e. 10 March 2020) and the time of our analysis (11 December 2020), with 25(OH)D concentration obtained by calculating the mean of the same period of the previous 2 years. Age and sex distribution of the outpatient population were neither significantly different in this period of the year 2020 compared with the same period of the previous 2 years. A modest but significantly lower likelihood (16.0% vs. 17.9%; odds ratio, 0.87; 95% CI, 0.80–0.96; P=0.003) of 25(OH)D deficiency (i.e. defined as a serum level <50 nmol/l or <20 ng/ml), was found in the year 2020 compared with the same period of the previous 2 years.

As also shown in table 1, significantly higher serum 25(OH)D values were observed during the 2020 lockdown period compared with the same period of the previous 2 years, a difference that was also associated with significantly higher prevalence of men, whilst the age of the outpatients was essentially comparable with that of the previous 2 years. During the 2020 lockdown period, the likelihood of testing people with 25(OH)D deficiency was further reduced (20.4% vs. 26.3%; odds ratio, 0.72; 95% CI, 0.57–0.90; P = 0.005). As concern the post-lockdown period, a modest but significantly lower serum 25(OH)D concentration was observed between late May and early December 2020, though the rate of 25(OH)D deficiency remained almost unchanged compared with the same period

Table 1 Sex distribution and median (and interquartile range) values of age and serum 25(OH)D concentrations of an outpatient population in year 2020 (from 10 March to 11 December 2020, stratified by COVID-19 lockdown and post-lockdown periods) compared with the same period of the previous 2 years (2018–2019)

Period	2020				2018–2019			
	n	Age (years)	Female (%)	25(OH)D (nmol/l)	n	Age (years)	Female (%)	25(OH)D (nmol/l)
10 March to 11 December	5008	65 (53–74)	3870/5008 (77.3%)	78.0 (58.8–97.3)	11 095	64 (52–74)	8571/11 095 (77.3%)	77.0 (57.4–97.8)
						P = 0.141	P = 0.972	P = 0.277
25(OH)D <- 50 nmol/l	801/5008 (16.0%)	-	-	-	1985/11 095 (17.9%)	-	-	-
Lockdown period (10	509	64 (53–73)	373/509 (73.3%)	78.2 (54.1–99.7)	2912	65 (52–75)	2310/2912 (79.3%)	71.3 (48.3–93.8)
March to 17 May) 25(OH)D <- 50 nmol/l						P = 0.083	P = 0.002	P = 0.002
	104/509 (20.4%)	-	-	-	767/2912 (26.3%)	-	-	-
Post-lockdown period (18	4499	65 (53–74)	3497/4499 (77.7%)	78.0 (59.2–97.2)	8183	64 (52–74)	6261/8183 (76.5%)	78.6 (59.9–98.8)
May to 11 December)						P = 0.024	P = 0.120	P = 0.009
25(OH)D <- 50 nmol/l	697/4499 (15.5%)	-	-	-	1218/8183 (14.9%)	-	-	-

Note: *P*-values for differences in age, gender distribution and serum 25(OH)D levels between years 2020 vs. 2018–2019. 25(OH)D, 25-hydroxyvitamin D.

of the previous 2 years (15.5% vs. 14.9%; odds ratio, 1.05; 95% CI, 0.95-1.16; P=0.360).

#### **Discussion**

There is common perception that the nationwide isolation measures imposed by the current COVID-19 pandemic outbreak may have been associated with lower sunlight exposure and a consequent surge in vitamin D, thus potentially jeopardizing population health. Nonetheless, the results of our analysis on serum 25(OH)D concentrations measured in a large outpatient adult population from the beginning of the Italian COVID-19 outbreak and the consequent lockdown period seemingly attest that the cumulative prevalence of 25(OH)D deficiency in our province has remained almost unchanged in 2020 compared with the previous 2 years. Nonetheless, a paradoxical increase of serum 25(OH)D, accompanied by reduced prevalence of 25(OH)D deficiency, has been observed during the COVID-19 lockdown period, counterbalanced by a small and probably clinically meaningless reduction of median serum 25(OH)D levels in the post-lockdown period. This paradoxical increase of serum 25(OH)D levels is not due to differences in age, but it is reasonable to assume that it might be in large part due to the higher proportion of men who measured their serum 25(OH)D levels during the 2020 lockdown period compared with the same period of the previous 2 years. This is in line with recent data from an Italian prospective cohort study, showing that serum 25(OH)D concentrations were significantly higher in men than in women in all body mass index classes, and decreased along with the increase of body mass index values.

Conflicts of interest: None declared.

### **Key points**

- Vitamin D concentration was not different in 2020 compared with the previous 2 years
- No increase prevalence of vitamin D deficiency was found during and after the lockdown period
- Lockdown did not produce clinically significant effects on vitamin D levels

#### References

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