

COVID-19 reminds us: community vitamin D deficiency



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COVID-19 reminds us: community vitamin D deficiency

Aim: *The aim of this study was to compare the vitamin D levels between the group of patients diagnosed with COVID-19 and healthy controls, and to investigate the relationship between vitamin D levels and various clinical findings.*

MATERIAL AND METHODS: *A total of 262 COVID-19-confirmed patients and 157 healthy controls were included in the study.*

RESULTS: *The mean vitamin D level in the COVID-19 group (12.8 ± 8.9 ng/mL) was significantly lower than the control group (15.2 ± 12.1 ng/mL) ($p=0.015$). The rate of those with vitamin D levels below 10 ng/mL in the COVID-19 group (49.6%) was significantly higher than the control group (39.5%) ($p=0.044$). In the logistic regression analysis, it was found that those with a vitamin D level below 10 ng/mL had a 1.508-fold increased risk of COVID-19 compared to those who had 10 ng/mL and above (Odds ratio: 1.01-2.252). According to the risk analysis, those who have vitamin D levels below 20 ng/mL are 1,224 times higher than those who have 20 ng/mL and above; those under 30 ng/mL were found to have an increased risk of 2.01 times compared to those of 30 ng/mL and above.*

CONCLUSIONS: *From the point of view of the literature data, we think that the findings we obtained may support researches that vitamin D level is significantly associated with both COVID-19 and other infections and many serious autoimmune and malignant diseases. As a result, rehabilitation programs on vitamin D deficiency should be organized and the society should be raised.*

KEY WORDS: Covid-19, Vitamin D25 (Oh) D

Introduction

Vitamin D is a fat-soluble vitamin that can be taken in food from outside and synthesized on the skin under the influence of ultraviolet rays from the sun. Cholecalciferol (vitamin D3) is of animal origin and ergocalciferol (vitamin D2) is of vegetable origin. 7-dehydrocholesterol, which is a cholesterol-like pre-molecule, is converted to pre-vitamin D, which is isomerized to

vitamin D3 with ultraviolet ray effect. Vitamins D3 and D2 are inactive, enzymatic conversion is required for them to be activated. First, it is subjected to 25-hydroxylation in the liver to 25(OH)D (calcidiol), which is the major circulating form of vitamin D; then it converts to 1,25(OH)₂D (calcitriol), the most active form of kidneys. This process is carried out by parathyroid hormone and some other intermediary molecules¹⁻³.

Although the main task of vitamin D and parathyroid hormone is related to bone metabolism, it has been reported to be related to the immune system and infections¹⁻⁴. Vitamin D receptor is found in B and T lymphocytes and mononuclear cells as well as many tissues in the body¹. Vitamin D deficiency has been shown to be associated with tuberculosis, asthma, and respiratory infections¹⁻⁴.

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It has been suggested that vitamin D affects the immune system and has an effect against infections³. According to this; 25(OH)D autocrine metabolism upregulates the expression of the signal vitamin D receptors and the 1-OHase enzyme when a macrophage or monocyte is stimulated by an infectious agent such as *Mycobacterium tuberculosis* through the toll-like receptor. A 25(OH)D level of 30 ng/ml or higher provides sufficient substrate to convert 25(OH)D to 1,25(OH)₂D in the mitochondria for the 1-OHase enzyme. 1,25(OH)₂D goes to the nucleus, where it enhances the expression of catelicidin, a peptide that can induce innate immunity and induce the destruction of infectious agents such as *M. tuberculosis*. It is also possible that 1,25(OH)₂D produced in monocytes or macrophages will have a local effect on activated T lymphocytes regulating cytokine synthesis and activated B lymphocytes regulating immunoglobulin synthesis³.

The threshold value for vitamin D deficiency has been defined as 20 ng/mL in some reports, 30 ng/mL in some and 10 ng/mL in others^{1,3}. In general, the definition of “insufficiency” for mild low level and “deficiency” for severe low level were used¹. It has been reported that vitamin D is produced at a sufficient level in light-skinned people by exposing the upper arm and face or arms, legs and hands to direct sunlight for 10 to 15 minutes at noon in spring, summer and autumn¹. It has been stated that vitamin D deficiency is becoming more common recently, therefore vitamin D deficiency should be called pandemic^{3,5,6}.

The Coronavirus Disease-2019 (COVID-19) pandemic caused by the SARS-CoV-2 of the new coronavirus has caused millions of cases and hundreds of thousands of deaths around the world. Studies have been conducted that vitamin D deficiency may be associated with the risk of developing COVID-19 or the prognosis or complications of COVID-19, and vitamin D supplementation may reduce these risks⁷⁻¹¹.

The aim of this study was to compare the vitamin D levels between the group of patients diagnosed with COVID-19 and healthy controls, and to investigate the relationship between vitamin D levels and various clinical findings.

Methods

This study was planned prospectively, approved by the local ethics committee, with *permission from the Ministry of Health*.

PATIENTS AND TESTS

The study included patients who were admitted to the clinics of our tertiary hospital with suspicion of COVID-19 and whose diagnosis was confirmed by molecular test-

ing, and those who were molecular-tested and found to be COVID-19 due to their contact history (262 patients in total) and 157 healthy individuals who applied to the hospital for various reasons. Clinical, laboratory and radiology findings of all participants were collected from central automation system records and analyzed.

STATISTICAL ANALYSIS

All statistical analyzes in the study were done using SPSS 25.0 software (IBM SPSS, Chicago, IL, USA).

Descriptive data are given as numbers and percentages. In terms of categorical variables, comparisons between groups were made with Pearson's Chi Square test and Fisher's Exact Test. Whether continuous variables are suitable for normal distribution was confirmed by the Kolmogorov-Smirnov Test. The differences between the groups in terms of continuous variables were analyzed using Student's t Test, and the comparison of mean values between multiple groups by variance analysis. The relationship between continuous variables was tested using Spearman's correlation analysis. Risk coefficient of categorical variables was evaluated by logistic regression analysis and given as “odds ratio”. The results were evaluated within the 95% confidence interval, and p<0.05 values were considered significant.

Results

Of the participants included in the study, 222 (52.5%) were male, and 197 (47.5%) were female. Patient and control groups were similar in terms of gender distribution (p=0.755). The mean age was 40.4±14.4 years (Age range 18-83 years) in the patient group, and was 38.8±15.4 years (Age range 19-77 years) in the control group and there was no significant difference between the groups (p=0.767).

25-OH vitamin D levels in serum were analyzed in three different ways as threshold values of 10 ng/mL, 20 ng/mL and 30 ng/mL. The rate of those with vitamin D levels below 10 ng/mL in the COVID-19 group (49.6%) was significantly higher than the control group (39.5%) (p=0.044). In the logistic regression analysis, it was found that those with a vitamin D level below 10 ng/mL had a 1.508-fold increased risk of COVID-19 compared to those who had 10 ng/mL and above (Odds ratio: 1.01-2.252). No significant difference was found between the groups in terms of the proportions of those with vitamin D levels below 20 ng/mL and those below 30 ng/mL (p=0.461 and p=0.062, respectively). According to the risk analysis, those who have vitamin D levels below 20 ng/mL had 1.224-fold higher risk than those who have 20 ng/mL and above; Those below 30 ng/mL were found to have an increased risk of 2.01-fold compared to those above 30 ng/mL (Table I)

TABLE I - Distribution of serum 25-OH vitamin D levels by COVID-19 and control groups. The threshold value for vitamin D was taken both 20 and 30 and analyzed separately.

	Control	COVID-19	Total	p	OR*
25-OH-D vitamin (threshold value=20)				0.044	1.508 (1.01-2.252)
<10	62 (39.5%)	130 (49.6%)	192 (45.8%)		
≥10	95 (60.5%)	132 (50.4%)	227 (54.2%)		
25-OH-D vitamin (threshold value =20)				0.461	1.224 (0.714-2.098)
<20	130 (82.8%)	224 (85.5%)	354 (84.5%)		
≥20	27 (17.2%)	38 (14.5%)	65 (15.5%)		
25-OH-D vitamin (threshold value =30)				0.062	2.010 (0.953-4.240)
<30	141 (89.8%)	248 (94.7%)	389 (92.8%)		
≥30	16 (10.2%)	14 (5.3%)	30 (7.2%)		

*OR: Odds ratio.

TABLE II - The mean 25-OH vitamin D levels according to COVID-19 presence, pneumonia finding, platelet and lymphocyte counts.

	n	Mean 25-OH vitamin D level (mg/dL)	SD	p
COVID-19 presence				0.015
Covid-19	262	12.8	8.9	
Control	157	15.3	12.1	
Pneumonia finding on CT				0.482
Present	89	13.1	10.5	
Absent	330	13.9	10.2	
Platelets				0.756
<150 bin /mm ³	11	11.9	6.3	
≥150 bin /mm ³	72	11.3	5.9	
Lymphocytes				0.293
<1000 /mm ³	13	9.8	5.2	
≥1000 /mm ³	70	11.7	6.0	

SD: Standard deviation

The mean vitamin D level in the COVID-19 group (12.8±8.9 ng/mL) was significantly lower than the control group (15.2±12.1 ng/mL) (p=0.015). There were no significant differences between those with and without signs of pneumonia on computed tomography (p=0.482), those with a platelet count below 150,000/mm³ (p=0.756), and those with a lymphocyte count below 1,000/mm³ and those below 1,000/mm³ and above (p=0.293) in terms of the mean vitamin D levels (Table II).

Discussion

Vitamin D deficiency came back to the agenda especially during the COVID-19 pandemic, which all people should stay at home. Although it is known that vitamin D has functions with some immune effects, it is a matter of debate whether these effects protect against

infections and especially COVID-19^{9,12}. Our study findings showed that there is a significant relationship between COVID-19 and vitamin D level.

Martineau et al.¹² reported that the elderly who were given high doses of vitamin D in their clinical study had a higher rate of upper respiratory infections compared to the placebo group, and the risk of infection increased, but the risk of lower respiratory infections did not change. Hansen et al.¹³ suggested that taking high vitamin D does not reduce or even increase the risk of respiratory infections. Hastie et al.¹⁴ reported that the level of vitamin D was not directly related to COVID-19. Rabbitt and Slattery¹⁵ stated that there is no evidence that vitamin D supplementation is an effective strategy against COVID-19. Contrary to these considerations; Ilie et al.⁹ examined the mean vitamin D levels in COVID-19 patients in European countries and determined that vitamin D levels were inversely proportional to both the number of cases and mortality, and stat-

ed that people with low vitamin D levels might have a higher risk for COVID-19 infection and mortality. Laird et al.¹⁶ reviewed the cases in European countries in their meta analysis and reported that there might be a relationship between vitamin D level and COVID-19. Grant et al.⁴ suggested that bringing the vitamin D level to around 40-60 ng/mL by administering high doses of vitamin D might reduce the risk of infection in individuals at high risk of COVID-19. Ebadi et al.¹⁰ and Hribar et al.¹¹ suggested that high doses of vitamin D could reduce the risks of poor prognosis and mortality in patients with COVID-19. Kara et al.⁶ stated that vitamin D deficiency and COVID-19-related mortality might be related. Jakovac¹⁷ suggested that polymorphisms in the vitamin D receptor genes in patients with COVID-19 could explain the unusual spreading behavior of COVID-19, and that vitamin D might be an alternative in the treatment of COVID-19. McCartney and Byrne¹⁸ stated that vitamin D supplements should be given to people especially at high risk of COVID-19. Panarese et al.¹⁹ and Tian et al.²⁰ stated that vitamin D deficiency and COVID-19 might be related. Zemb et al.²¹ stated in their extensive meta-analysis that vitamin D deficiency was observed very common due to less exposure to sunlight, especially in cold months, and that daily dose of vitamin D supplements at moderate doses was cheap and safe. These researchers also found that vitamin D reduces the frequency of acute respiratory infections, and that there was a relationship between vitamin D deficiency and COVID-19, although there was insufficient evidence, suggesting that people's staying at home during the COVID-19 pandemic might have increased vitamin D deficiency. Aygün⁷ claimed that Vitamin D could reduce organ and lung damage caused by COVID-19 (i) by decreasing COVID-induced cytokine storm by suppressing some interleukins from inflammatory cytokines, tumor necrosis factor-alpha (TNF-alpha) and gamma interferon (IFN-gamma), (ii) by increasing the production of the catelicid, which has a protective effect against lung damage, (iii) by decreasing the production of angiotensin-converting enzyme-2 (ACE-2), the entry-receptor of COVID-19, and (iv) by decreasing the accumulation of angiotensin-2 which is effective in lung damage in COVID-19. Molloy and Murphy²² suggested that vitamin D could provide protection against COVID-19 and its complications by increasing the levels of catelicides and decreasing cytokine levels. Mitchell²³ suggested that vitamin D might be protective against COVID-19 and organ damage by promoting the production of antimicrobial peptides in the airways and reducing the inflammatory response to infection. Faul et al.⁸ found that the mean vitamin D level measured at the time of admission to the hospital in patients with acute respiratory failure syndrome (ARDS) was significantly lower compared to patients without ARDS. In our study, the mean vitamin D level in the COVID-

19 group (12.8 ± 8.9 ng/mL) was significantly lower than the control group (15.2 ± 12.1 ng/mL) ($p=0.015$). The rate of those with vitamin D level below 10 ng/mL in the COVID-19 group (49.6%) was found to be significantly higher than the control group (39.5%) ($p=0.044$). In the logistic regression analysis, it was found that those with a vitamin D level below 10 ng/mL had a 1.508-fold increased risk of COVID-19 compared to those with 10 ng/mL and above (Odds ratio: 1.01-2.252). No significant difference was found between the groups in terms of the rates of those with vitamin D levels below 20 ng/mL and those below 30 ng/mL ($p=0.461$ and $p=0.062$, respectively). According to the risk analysis, those who have vitamin D levels below 20 ng/mL had 1.224-fold higher risk than those who have 20 ng/mL and above; Those below 30 ng/mL were found to have an increased risk of 2.01-fold compared to those above 30 ng/mL. These findings show that vitamin D levels are associated with COVID-19. According to these data, those who have low vitamin D levels have a higher risk of COVID-19. In addition, the findings obtained from the very low vitamin D threshold show that very low vitamin D levels increase the risk, and very high levels may protect against COVID-19. Further and larger studies should be conducted using different vitamin D threshold levels.

In our study, there were no significant differences between those with and without signs of pneumonia on computed tomography ($p=0.482$), those with a platelet count below $150,000/\text{mm}^3$ and those below $150,000/\text{mm}^3$ ($p=0.756$), those with a lymphocyte count below $1,000/\text{mm}^3$ and those below $1,000/\text{mm}^3$ and above ($p=0.293$) in terms of the mean vitamin D levels. These findings suggest that there is no relationship between the vitamin D level of COVID-19 radiology and laboratory findings and vitamin D level.

There were some limitations in our study. Since the study was carried out for cross-sectional purposes, it was not possible to determine whether patients had relapses or reinfections in the long term, and their relationship with vitamin D levels could not be analyzed.

The data obtained show that vitamin D deficiency is an important and common public health problem and the society should be made conscious about this issue. It appears that vitamin D deficiency may increase due to the decrease in sun exposure and inadequacy of foods, especially during COVID-19 pandemic, which cannot be taken outdoors, and additional supplements are required. Due to the COVID-19 pandemic, vitamin D levels should be closely monitored and supplemented, especially in people over 65 years of age who have to stay at home for a long time to reduce the risk of both general health and infection.

From the point of view of the literature data, we think that the findings we obtained may support researches that vitamin D level is significantly associated with both COVID-19 and other infections and many serious

autoimmune and malignant diseases. As a result, rehabilitation programs on vitamin D deficiency should be organized and the society should be raised.

Riassunto

Il nostro scopo è quello di confrontare i livelli di vitamina D tra il gruppo di pazienti con diagnosi di COVID-19 e controlli sani e di indagare la relazione tra i livelli di vitamina D e vari risultati clinici includendo nello studio 262 pazienti confermati COVID-19 e 157 controlli sani.

RISULTATI: Il livello medio di vitamina D nel gruppo COVID-19 ($12,8 \pm 8,9$ ng / mL) era significativamente inferiore rispetto al gruppo di controllo ($15,2 \pm 12,1$ ng / mL) ($p = 0,015$). Il tasso di quelli con livelli di vitamina D inferiori a 10 ng / mL nel gruppo COVID-19 (49,6%) era significativamente più alto rispetto al gruppo di controllo (39,5%) ($p = 0,044$). Nell'analisi della regressione logistica, è stato scoperto che quelli con un livello di vitamina D inferiore a 10 ng / mL avevano un rischio aumentato di 1,508 volte di COVID-19 rispetto a quelli che avevano 10 ng / mL e oltre (Odds ratio: 1,01-2,252). Secondo l'analisi del rischio, coloro che hanno livelli di vitamina D inferiori a 20 ng / mL sono 1.224 volte più alti di quelli che hanno 20 ng / mL e oltre; quelli sotto i 30 ng / mL hanno riscontrato un rischio aumentato di 2,01 volte rispetto a quelli di 30 ng / mL e superiori.

CONCLUSIONI: Dal punto di vista dei dati della letteratura, riteniamo che i risultati che abbiamo ottenuto possano supportare le ricerche secondo cui il livello di vitamina D è significativamente associato sia con COVID-19 che con altre infezioni e molte gravi malattie autoimmuni e maligne. Di conseguenza, dovrebbero essere organizzati programmi di riabilitazione sulla carenza di vitamina D e la società ne dovrebbe essere avvantaggiata.

References

- Chang SW, Lee HC: *Vitamin D and health-The missing vitamin in humans*. *Pediatr Neonatol*, 2019; 60(3): 237-44.
- Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al.: *Vitamin D supplementation for prevention of mortality in adults*. *Cochrane Database Syst Rev*, 2014; (1): CD007470.
- Holick MF: *The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention*. *Rev Endocr Metab Disord*, 2017; 18(2): 153-65.
- Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, et al.: *Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths*. *Nutrients*, 2020; 12(4): 988.
- Fidan F, Alkan BM, Tosun A. *Pandemic Era: Vitamin D Deficiency and Insufficiency*. *Türk Osteoporoz Dergisi*, 2014; 20: 71-4.
- Kara M, Ekiz T, Ricci V, Kara Ö, Chang KV, Özçakar L: *Scientific Strabismus or Two Related Pandemics: COVID-19 & Vitamin D Deficiency* [published online ahead of print, 2020 May 12]. *Br J Nutr*, 2020; 1-20.
- Aygun H: *Vitamin D can prevent COVID-19 infection-induced multiple organ damage* [published online ahead of print, 2020 May 25]. *Naunyn Schmiedebergs Arch Pharmacol*, 2020; 1-4.
- Faul JL, Kerley CP, Love B, O'Neill E, Cody C, Tormey W, et al.: *Vitamin D Deficiency and ARDS after SARS-CoV-2 Infection*. *Ir Med J*, 2020; 113(5): 84.
- Ilie PC, Stefanescu S, Smith L: *The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality* [published online ahead of print, 2020 May 6]. *Aging Clin Exp Res*, 2020; 1-4.
- Ebadi M, Montano-Loza AJ: *Perspective: Improving vitamin D status in the management of COVID-19* [published online ahead of print, 2020 May 12]. *Eur J Clin Nutr*, 2020; 1-4.
- Hribar CA, Cobbold PH, Church FC: *Potential role of vitamin d in the elderly to resist COVID-19 and to slow progression of parkinson's disease*. *Brain Sci*, 2020; 10(5): E284.
- Martineau AR, Hanifa Y, Witt KD, Barnes NC, Hooper RL, Patel M, et al.: *Double-blind randomised controlled trial of vitamin D3 supplementation for the prevention of acute respiratory infection in older adults and their carers (ViDiFlu)*. *Thorax*, 2015; 70(10): 953-60.
- Hansen KE, Johnson MG: *An update on vitamin D for clinicians*. *Curr Opin Endocrinol Diabetes Obes*, 2016; 23(6): 440-4.
- Hastie CE, Mackay DF, Ho F, Celis-Morales CA, Katikireddi SV, Niedzwiedz CL, et al.: *Vitamin D concentrations and COVID-19 infection in UK Biobank*. *Diabetes Metab Syndr*, 2020; 14(4): 561-65.
- Rabbitt L, Slattery: *Vitamin D and Covid-19: A Note of Caution*. *Ir Med J*, 2020; 113(5): 82.
- Laird E, Rhodes J, Kenny RA: *Vitamin D and Inflammation: Potential Implications for Severity of Covid-19*. *Ir Med J*, 2020; 113(5): 81.
- Jakovac H: *COVID-19 and vitamin D-Is there a link and an opportunity for intervention?* *Am J Physiol Endocrinol Metab*, 2020; 318(5): E589.
- McCartney DM, Byrne DG: *Optimisation of Vitamin D Status for Enhanced Immuno-protection Against Covid-19*. *Ir Med J*, 2020;113(4):58.
- Panarese A, Shahini E: *Letter: Covid-19, and vitamin D*. *Aliment Pharmacol Ther*, 2020; 51(10): 993-95.
- Tian Y, Rong L: *Letter: Covid-19, and vitamin D. Authors' reply*. *Aliment Pharmacol Ther*, 2020; 51(10): 995-6.
- Zemb P, Bergman P, Camargo CA, Cavalier E, Cormier C, Courbebaisse M, et al.: *Vitamin D deficiency and COVID-19 pandemic* [published online ahead of print, 2020 May 28]. *J Glob Antimicrob Resist*, 2020; S2213-7165(20)30132-6.
- Molloy EJ, Murphy N: *Vitamin D, Covid-19 and Children*. *Ir Med J*, 2020; 113(4): 59.
- Mitchell F: *Vitamin-D and COVID-19: do deficient risk a poorer outcome?* [published online ahead of print, 2020 May 20]. *Lancet Diabetes Endocrinol*, 2020; S2213-8587(20)30183-2.

Commento e Commentary

PROF. NICOLA PICARDI

Già Ordinario di Chirurgia Generale

L'argomento trattato è ai limiti degli interessi per una rivista di chirurgia, ma l'osservazione è comunque da tenere presente per più di un motivo, perché non è detto che si tratti solamente di una osservazione isolata. Pertanto si è deciso di pubblicare l'articolo.

Innanzitutto è ancora troppo presto per ipotizzare se gli squilibri dei livelli di vit D siano una causa favorente l'infezione o il contagio da Covid oppure siano una conseguenza del contagio avvenuto. Inoltre dati gli stretti rapporti tra vit D ed il metabolismo del Calcio/Fosforo sarebbe interessante indagare più ampiamente la problematica, studiando anche l'assetto elettrolitico in generale – in particolare Ca, P, Mg – e i livelli del paratormone sia durante la malattia conclamata, ma anche nel follow up di pazienti guariti. Non è detto che ne scaturisca un quadro interpretativo con riflessi pragmatici, ma le innata curiosità dei medici è portata a indagare e spaziare possibilmente senza limiti dettati dai costi di una simile impresa. Più si conosce, maggiori sono le probabilità di poter incidere sul decorso della malattia.

In un momento in cui le conoscenze del coronavirus in questione e delle sue varianti sono ancora episodiche, e le osservazioni circa la variabile efficacia nei malati di farmaci sostanzialmente anti-infiammatori ancora non del tutto definite, il livello di Vit D può rappresentare un tassello aggiuntivo alla conoscenza di una patologia complessa e sotto osservazione, con imprevedibili riflessi anche sul possibile effetto dei vaccini in sperimentazione.

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The topic is at the limits of interests for a journal of surgery, but it was decided to publish the article anyways, as the observation is to be kept in mind for more than one reason. We do not know if it is an isolated observation, and it is possible that a surgical therapy may also be necessary in Covid 19 patients.

First of all, it is still too early to know whether the imbalances of the vit D levels are a favoring cause of the Covid infection or simple contagion or are a consequence of the same infection. Furthermore, given the close relationships between vit D and the metabolism of Calcium / Phosphorus it would be interesting to investigate widely the problem more, studying also the electrolytic situation in general – in particular Ca^{++} , Mg^{++} – and the levels of the parathyroid hormone both during the full-blown disease, with explosion of inflammatory mechanisms, but also in the follow up of recovered patients. An interpretative framework with pragmatic reflexes does not necessarily emerge, but the physicians' innate curiosity leads to investigate deeply and possibly without range limits of costs and organization. The more you know, the more likely you could be able to affect the course of the disease.

At a time when the knowledge of the coronavirus and its variants are still episodic, and the observations about the variable efficacy in patients with substantially anti-inflammatory drugs still not fully defined, the level of Vit D can represent an additional element to the knowledge of a complex pathology and under observation, perhaps trivial and without decisive meaning, and also without reflections on the possible effects of the vaccines under development.