World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(Research Article)

Check for updates

The possible impact of COVID-19 pandemic on serum vitamin D levels on newborns in Greece

Artemisia Kokkinari [1,*], Maria Dagla [1], Aikaterini Lykeridou [1], Kostas Bagianos [2], Evangelia Antoniou [1] and Georgios Iatrakis [1]

[1] *Department of Midwifery, School of Health & Care Sciences, University of West Attica, Athens, 12243, Greece.*
[2] *Biochemical Department of Tzaneio Piraeus General Hospital, Piraeus, Greece.*

World Journal of Advanced Research and Reviews, 2023, 20(03), 1405–1413

Publication history: Received on 05 November 2023; revised on 18 December 2023; accepted on 20 December 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.20.3.2558

Abstract

Background: Very few studies have evaluated the probable role of the period of 2019 coronovirus disease (COVID-19) pandemic on neonatal 25(OH)D levels. Vitamin D status in the fetus and newborn is largely determined by the vitamin D status of the mother. A recent study in Greece witnessed an unexpected rise in maternal 25(OH)D levels in pregnancy during the COVID-19 period. Consequently, it remains unclear whether neonatal 25(OH)D levels decreased due to reduced sun exposure in the COVID-19 period or followed their unexpected maternal findings.

Methods: We studied neonatal 25(OH)D levels in cord blood specimens at birth in 246 neonates of Greek mothers with stratified random sampling, from September 2019 to January 2022. We divided our samples into the pre-COVID-19 period and the post-COVID-19 period. Chi-square test was used to find an association between neonatal 25(OH)D concentrations throughout the COVID-19 period. Quantitative results of 25(OH)D vitamin levels on newborns were transformed into qualitative variables assessing lack of 25(OH)D, adequacy, deficiency and severe deficiency and thus defined in that way. All other results of 25(OH)D levels are presented as means ± standard deviations (SD) or by frequencies and percentages.

Results: The results in neonates exhibited a similar pattern to that of their mothers'. The mean serum values of 25(OH)D levels of the newborns were statistically significantly higher during the COVID-19 period compared to the pre-COVID-19 period.

Conclusions: Although during the COVID-19 period lower maternal and therefore neonatal 25(OH)D levels were expected, these were higher and because of these findings, we can only make assumptions. Without a doubt, further investigation is required.

Keywords: Pregnancy; Vitamin D Levels; Neonatal 25(OH)D Levels; Infants; COVID-19

1. Introduction

Globally, in December 2019, a rapidly spreading, severe virus causing a particularly severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged as the 2019 coronavirus disease (COVID-19) [1]. Greek government took controlling measures known as lockdown. The new reality in Greece, lockdown, came into force on March 23. Lockdown in our country lasted 42 days (March 23 to May 4). Despite the importance of these controlling measures, during the COVID-19 pandemic, prolonged confinement at home could adversely affect the health and development of individuals.

* Corresponding author: Artemisia Kokkinari.

Thus, people who are confined to their homes for long periods of time, since they are more likely to exercise less, eat unhealthily, and get less exposure to sunlight, may put them at greater risk of vitamin D deficiency (VDD) [2,3,4].

Vitamin D is a fat-soluble vitamin with numerous actions. Vitamin D is enzymatically converted in the liver to 25-hydroxyvitamin D (25(OH)D), the main form of circulation of vitamin D [5]. A person's vitamin D adequacy can be assessed by measuring serum 25(OH)D concentrations. Vitamin D3 production is mainly through skin synthesis when the skin's 7-Dehydrocholesterol (7-DHC) is exposed to the sun's ultraviolet (UV) light, 290-315 nm [5]. There are two (commercially) available forms, D2 (ergocalciferol) and D3 (cholecalciferol). Despite the importance of this vitamin for health, VDD, throughout the Western world, is very common. In fact, regarding this issue, there was recent talk of a "European pandemic" [6]. Contrary to expectation, for eastern and southern Mediterranean regions and despite apparent sunshine, a high prevalence of low vitamin D status is observed [7]. Some researchers suggest that adequate vitamin D synthesis requires 5-30 minutes of sun exposure, without sunscreen, especially between 10 am and 4 pm, daily or at least twice a week, on the face, hands, or arms and legs [8, 9]. The results of a Greek study by Papadakis et al [10], show a strong correlation between season and a given latitude, highest of the tropics (Athens, Greece: 37.9° North (N) of the Equator), with serum 25(OH)D concentrations. Given this condition, the lowest 25(OH)D levels in serum concentrations are observed during the winter and early spring months. From a climatic point of view, the year can be divided into two main seasons, the cold and rainy season that lasts from mid-October to the end of March and the hot and dry season that lasts from April to October (Hellenic National Meteorological Service/HNMS) [11]. Inadequate radiation or insufficient cutaneous absorption of UVB is one of the cardinal causes of VDD [12]. Season, time of day, cloud cover, smog, skin melanin content, and sunscreens are among the factors that influence UV exposure and vitamin D synthesis [13]. Sunlight exposure results in sustained levels of available 25(OH)D concentrations, compared to orally administered vitamin D supplementation [14]. The contribution of vitamin D3 from dietary sources is less important because foods containing vitamin D3 are not daily dietary choices [5]. At times, there has been much debate as to whether vitamin D intake from the diet or from a supplement is the same as skin production of vitamin D3 [15]. It has been observed that vitamin D3 produced in the skin lasts 2-3 times longer in the blood stream, compared to its oral ingestion [15].

According to studies, the prevalence of VDD in the general population is very important and pregnancy is one of the known risk factors (RFs) for this deficiency, and in general VDD has been reported between 47 and 83% in black and white pregnant women respectively [16]. Vitamin D status in the fetus and newborn is largely determined by the vitamin D status of the mother [16]. Since VDD is prevalent in mothers, many infants are also at risk of deficiency and insufficiency of vitamin D levels [16]. Therefore, when we assume that mothers will suffer much more from VDD, during the corona period, due to theoretically less sun exposure that deteriorate vitamin D synthesis to the skin, with the same rationale we imagine that newborns will suffer the same, due to the quarantine and restrictions on movement from home. Although infant exposure to UVB radiation can produce vitamin D, the American Academy of Pediatrics (AAP) advises parents to keep infants under 6 months out of direct sunlight, wear protective clothing, hats and apply sunscreen to small areas of exposed skin when sun exposure is unavoidable [17]. Vitamin D content of human milk is related to maternal vitamin D concentrations [18]. Most research provides evidence that breast milk has many unique characteristics, with many strong maternal and environmental influences, than previously recognized [19]. Neither excessive maternal intake of nutrients, including vitamin D, nor moderate, inadequate dietary intake is capable of appreciably affecting nutrient transfer to infants unless it persists for a long time [19]. COVID-19 and the resulting lockdown have reduced traffic load and therefore air pollution levels. Atmospheric pollution is one of the main factors that determine the extent of solar UVB radiation reaching the earth's surface resulting in insufficient radiation, which leads to reduced skin synthesis of vitamin D [20].

We evaluated neonatal 25(OH)D levels at birth. This study was conducted to evaluate the role of the COVID-19 period on 25(OH)D levels of neonates born to Greek mothers or to mothers living in Greece for the past ten years taking into account the administration or not of prenatal vitamin D supplements during pregnancy, the role of the season and the hours of sunshine. The aim was to determine whether neonatal 25(OH)D levels exhibited a similar unexpected rise in maternal 25(OH)D levels during the pandemic period found in a previous study of ours [21].

2. Materials and methods

We conducted a cross-sectional study of 246 neonates of Greek mothers or mothers who had lived in Greece for more than 10 years. These neonates were born in the obstetrics and gynecology clinic of the Tzaneio General Hospital of Piraeus, from September 2019 until January 2022. We studied serum 25(OH)D levels on the newborn at birth, with stratified random sampling. The study was performed on neonatal cord blood samples that were always collected at birth, immediately after ligation, at the end of labor. Circulating levels of neonatal 25(OH)D in full-term pregnancies (after the 37th week) were studied. The exclusion criteria were neonates from pregnant women who were taking medicine that could potentially affect vitamin D levels (corticosteroids, anticonvulsants, antituberculars, antifungals), or were being given higher doses of supplement 25(OH)D (>800 IU). Also excluded were neonates from pregnant women with a known history of rheumatoid arthritis, thyroid, parathyroid or adrenal disorders, liver or kidney failure, metabolic bone disease, DM type 1 and malabsorption syndromes (pancreatic insufficiency, fibrocystic disease and celiac disease).

Immunological tests were used to measure neonatal 25(OH)D levels. All other information related to the presence or absence of factors influencing neonatal 25(OH)D levels to the pre and post COVID-19 period were drawn from a detailed medical history and a personal questionnaire that were accompanying each mother's results. We divided our samples into the pre-COVID period (September 2019 to March 2020) and the post-COVID period (March 2020 and beyond). We assessed maternal 25(OH)D concentrations in pregnancy, as well as intake or non-prenatal vitamin D supplementation, alone or in combination with other vitamins or metals (Ca, Mg, Zn). Season group, smog, skin melanin content, and sunscreens were among the factors also assessed as potentially influencing UV exposure and vitamin D synthesis. The data collected were assessed by two researchers to improve the quality of the research. Bibliography was searched in international databases such as PubMed, Web of Science, Cochrane Library and Embase, to identify relevant studies without restriction on language, population or year. We searched for studies assessing any effects of COVID-19 period on neonatals levels of 25(OH)D in all countries including Greece.

Our samples were divided into two seasonal periods, the cold and rainy one lasting from mid-October to the end of March, named group A and the hot and dry season lasting from April to October, named group B. Neonatal 25(OH)D concentrations were evaluated according to the American Endocrine Society. The newborns of the mothers of each category were also divided into newborns with: a) adequate levels of vitamin 25(OH)D (>30 ng/ml) [22], b) vitamin 25(OH)D deficiency (16-29 ng/ml), c) lack of vitamin 25(OH)D (<15 ng/ml) [22] again according to the adequacy criteria of the American pediatric endocrine society (Table 1). As in adults, one more category could be added: d) severe vitamin deficiency 25(OH)D (≤12.5 ng/ml) [23] or 25(OH)D (<10ng/ml) given the most recent review of Braegger et al [24]. A deficiency and severe deficiency of 25(OH)D was defined for clinical hypovitaminosis.

Data were processed using IBM SPSS statistics 26 software. Chi-square test was used to find an association between neonatal 25(OH)D concentrations within the COVID-19 period. Quantitative results of 25(OH)D vitamin levels on the newborn were converted to qualitative variables assessing lack of 25(OH)D, adequacy, deficiency and severe deficiency of neonatal concentrations and thus defined in that way. Also, the means ± standard deviations (SD) of neonatal 25(OH)D levels are presented by frequencies and percentages. A statistical test was performed to check for the existence of statistical significance. The normality of the sample was tested. The neonatal 25(OH)D values did not follow a normal distribution, therefore, in order to study whether there is a statistically significant difference in the mean values, of the pre- and the post-COVID-19 period, the non-parametric Mann-Whitney U test was used. All p-values less than 0.05 (P ≤0.05) were defined as statistically significant. We also carried out two multiple regression analyses in our study, one for the pre-COVID-19 period and one for the post-COVID-19 period in order to examine other contributory factors in neonatal 25(OH)D levels. Multiple regression model was used to assess the association between neonatal 25(OH)D levels with the other factors that could potentially influencing UV exposure and vitamin D synthesis (season group, smog, skin melanin content, vitamin D intake and sunscreens). As we said these analyses were recorded in two separate tables one for the pre-COVID-19 period and one for the post-COVID-19 period. Each analysis had neonatal 25(OH)D levels as a dependent variable. In each table, we included the season group, smog, skin melanin content, pregnant women's vitamin D intake and sunscreens as independent variables. The result of the analysis in each table could predict the probability of each independent variable influencing the respective neonatal 25(OH)D levels. To determine the statistical significance of each independent variable, the p value ≤0.5 was considered.

3. Results

A statistical study was performed to demonstrate whether newborns' 25(OH)D levels differed in the pre-COVID-19 versus post-COVID-19 period. Our sample involved 92 newborns, from the pre-COVID-19 period and 154 newborns in the COVID-19 period. In the pre-COVID-19 period, the mean of neonatal 25(OH)D levels was 12.88 ± 8.70 ng/ml (95%CI: 11.09 - 14.68) and in the post-COVID-19 period was 15.42 ± 8.27 ng/ml (95%CI: 14.10 - 16.73) (Table 1). The Mann-Whitney U test showed that the difference in mean values between neonatal 25(OH)D levels in the pre- and the post-COVID-19 period was statistically significant (Table 2). Because the P value (P) was P =0.005 that it was <0.05, the null hypothesis that the mean values of the two samples were the same was rejected. Therefore, the existence of a statistically significant difference in the average values, of the neonatal 25(OH)D levels, in the pre- and the post-COVID-19 period was proved.

As we said we also carried out two multivariate analyses in our study, one for the pre-COVID-19 period and one for the post-COVID-19 period in order to examine other contributory factors in neonatal 25(OH)D levels. In these analyses we assessed maternal intake or not of supplemental vitamin D, the seasonal group that the neonates belonged to, dependent on when they were born, skin type of the mother, smoking and alcohol consumption all of which could influence to neonatal 25(OH)D levels. In this way we investigated other parameters that possibly co-determined neonatal 25(OH)D levels. In the pre-COVID-19 period, maternal skin colour (P =0.026), intake or not of supplemental vitamin D by pregnant mothers (P =0.015) and seasonal period (P =0.035) seemed to contribute to neonatal 25(OH)D levels as their P value was <0.05% and therefore statistically significant. However, after adjusting for the covariates, the impact of the COVID-19 period on neonatals 25(OH)D levels is evident and statistically significant only for supplemental vitamin D intake during pregnancy (P =0.000). It seems that a smoking mother (P =0.052) is marginally statistically not significant while season (P =0.082) and skin pigmentation (P =0.545) are both statistically not significant all of which do not seem to influence neonatal 25(OH)D levels.

Table 1 Comprehensive display of all the statistics on the newborn 25(OH)D levels, for the pre-COVID-19 period and the COVID-19 period

Descriptives for the pre-COVID 19 period				
			Statistic	Std. Error
neonatal_25(OH)D	Mean		12.8828	0.90313
	95% Confidence Interval for Mean	Lower Bound	11.0891	
		Upper Bound	14.6765	
	5% Trimmed Mean		11.9429	
	Median		11.6000	
	Variance		75.855	
	Std. Deviation		8.70946	
	Minimum		1.40	
	Maximum		51.00	
	Range		49.60	
	Interquartile Range		10.05	
	Skewness		2.073	0.250
	Kurtosis		6.599	0.495
Descriptives for the COVID-19 period and after				
			Statistic	Std. Error
neonatal_25(OH)D	Mean		15.4174	0.66416
	95% Confidence Interval for Mean	Lower Bound	14.1054	
		Upper Bound	16.7295	
	5% Trimmed Mean		14.8430	
	Median		14.0000	
	Variance		68.372	
	Std. Deviation		8.26877	
	Minimum		3.40	
	Maximum		45.80	
	Range		42.40	

	Interquartile Range	11.30	
	Skewness	1.055	0.195
	Kurtosis	1.249	0.387

Table 2 Mann-Whitney U Test

	Neonatal 25(OH)D
Mann-Whitney U	5659.000
Wilcoxon W	10030.000
Z	-2.831
Asymp. Sig. (2-tailed)	0.005

	COVID-19	**N**	**Mean Rank**	**Sum of Ranks**
Neonate's 25(OH) D	pro COVID-19 period	92	107.85	10030.00
	post COVID-19 period	154	134.49	20846.00
	Total	246		

Table 3 The multiple regression analysis of neonatal 25(OH)D levels in the pre-COVID-19 period and the COVID-19 period. Neonatal 25(OH)D levels in the pre-COVID-19 period

Model		**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**
		B	Std. Error	Beta		
1	(Constant)	20.943	5.810		3.604	0.001
	Intake of vitamin D	4.901	1.966	0.260	2.493	0.015
	Seasonal Group	-2.308	2.459	-0.095	-0.939	0.031
	Skin melanin content	-4.735	2.090	-0.230	-2.265	0.026
	Smoking	-0.311	1.162	-0.027	-0.268	0.789
	Sunscreen	0.644	1.414	0.047	0.456	0.650
a. Dependent Variable: neonatal_25(OH)D levels						

Neonatal 25(OH)D levels in the COVID-19 period and after						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	18.066	3.259		5.543	.000
	Intake of vitamin D	4.730	1.305	0.276	3.624	.000
	Seasonal Group	-2.261	1.290	-0.133	-1.753	.082

	Skin melanin content	-.890	1.466	-0.048	-0.607	.545
	Smoking	1.561	0.796	0.153	1.961	0.052
	Sunscreen	-1.980	1.166	-0.136	-1.699	0.091

Dependent Variable: neonatal_25(OH)D levels

4. Discussion

The purpose of our study was to determine neonatal 25(OH)D levels at birth in a sunny Mediterranean country like Greece and to assess the role of COVID-19 period on neonatal 25(OH)D levels. Our results show that neonatal 25(OH)D levels increased during the post-COVID-19 period, consistent with an increase in maternal 25(OH)D levels that was seen in the study of Kokkinari et al [21]. The mean value of the neonatal 25(OH)D levels, after COVID-19, was 2.54 units higher than the mean of neonatal 25(OH)D levels in the pre-COVID-19 period. Yet, it is unknown what triggered the increased maternal and neonatal levels of 25(OH)D levels during the pandemic period.

There is no other published study during the period pertaining to neonatal 25(OH)D levels and consequently we are unable to compare our results with other similar studies. Whatever studies concerning neonates during the COVID-19 period referred to two-month-old neonates and above and as a result we are unable to compare the results with ours since at the age of two-months there are many more factors besides maternal 25(OH)D levels that have an impact on neonatal 25(OH)D levels such as their diet (breastfeeding or milk formulas) and their exposure to the sun. In the multivariate analyses of both the pre and post-COVID-19 periods another paradox was observed. The seasonal group that the neonates belonged to and maternal skin pigmentation were found to be non-statistically significant prognostic factors for increase in neonatal 25(OH)D levels. Therefore season and related sunlight during the COVID-19 period left neonate 25(OH)D levels unaffected something which definitely did not occur in the pre-COVID-19 period. Yu et al [25] noticed, as we did, a disorder in the annual variability of 25(OH)D levels that lacked, as in our study, the characteristic seasonality of 25(OH)D levels during the pandemic. What is perplexing is what was it that increased maternal and neonatal 25(OH)D levels during the corona-virus period, as what we knew to date about the involvement of sunshine, seasonality and skin pigmentation did not seem to apply to this period. On the contrary, these factors seem to leave 25(OH)D levels unaffected. What we also do not know is whether neonatal 25(OH)D levels, in this particular period of the coronavirus, increased because of the increase in 25(OH)D of their mothers, or whether the fetus-neonates themselves developed, for some reason, a separate pathway of 25(OH)D metabolism through the placenta. All this requires further research and well-devised and organized studies.

During the COVID-19 it is credible to assume that the Corona-virus period brought about changes in people's habits and these are probably responsible for the increase in neonatal 25(OH)D levels. The paradoxical fact of higher vitamin D on the newborns, in the COVID-19 period, could it be the change in the mother's habits during the pandemic, the improvement in the quality of air (the reduction in air pollution) and other unexplored factors contributed to improved 25(OH)D levels. Expectant mothers, sent the required SMS messages to allow them, to get out of their house, for physical exercise or individual sports. If we combine the fact that this walk or exercise was taken in the morning hours, since physical presence at work had been suspended and most people carried out their work mainly online, there was flexibility for these activities or sports to be done in the morning hours and to benefit from the advantages of the sun, resulting in an abundant production of vitamin D in the skin [23]. An another possible reason for the higher vitamin D levels in expectant mothers and thus in their newborns, in this period, may have been their fear of contracting COVID-19 and therefore being more regular in taking vitamin D or taking multivitamin supplements with vitamin D [21]. Finally, another possible explanation is the fact that immunity of the mother-newborn couple, during the sensitive COVID-19 period, may have increased either due to a possible previous illness of the mothers from Corona-virus or due to the vaccination of a large part of the pregnant women who may have also affected neonates and triggered an increase in both maternal and neonatal 25(OH)D levels since 25(OH)D is associated with the immune response [26] of the mother and perhaps through an additional activation path of vitamin D metabolism across the placenta. Therefore, more studies are necessary, in order to have reliable results. More studies, involving the mother-newborn pair are also necessary, in populations that have been vaccinated or are for some reason in an immune response state in order to cross-check whether there is an increase in neonatal 25(OH)D levels. In our own study in the Corona-virus period, our questionnaire was designed in the pre-Coronavirus period and as such did not have the provision to record which pregnant women had been ill, which were vaccinated and if these are a function of increased 25(OH)D levels. Also, the correlation between maternal and neonatal 25(OH)D levels should be clarified, in periods when an increased immune response is needed, in order to create new prenatal programs aimed at supporting maternal and neonatal 25(OH)D concentrations with aim for more improved outcomes for mother and infant.

Therefore, more studies in Greece are necessary, in order to have reliable results.

5. Conclusions

Our study sought to assess the status of neonatal 25(OH)D levels and the role of COVID-19 on them at birth in a sample of neonates born to Greek mothers in a Mediterranean country such as Greece, which benefits from abundant sun in the synthesis of vitamin D. Our results showed that neonatal 25(OH)D levels increased in the post-COVID-19 period. If we accept the positive correlation between maternal and neonatal 25 levels reported by a number of studies, our results seem to be in agreement with the study by Kokkinari et al [21] which revealed an increase in maternal 25(OH)D levels. As we said before, it is unknown what triggered the elevated neonatal levels of 25(OH)D during the pandemic period. If this is indeed the case, it is quite possible to hypothesize a possible protective effect of high levels of vitamin D in preventing not only the period of the coronavirus involved in a severe course of inflammation but also for any inflammatory condition. More studies, involving the mother-newborn pair are also necessary, in populations that have been vaccinated or are for some reason in an immune response state in order to cross-check whether there is an increase in neonatal 25(OH)D levels. If the increase in neonatal 25(OH)D concentrations during a period of increased immunological demands is finally confirmed, it is very likely that an administered vitamin D supplement to the mothers, amount and dose that remains to be clarified with other further studies, would be beneficial.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

The scientific council of Tzaneio Hospital, Piraeus resulted from elections concluded on 3/28/2018 and was constituded in a body with Act Number 5844 of 29-3-2018 of the Director of the hospital. The scientific council, in accordance with strictly observing conditions of anonymity and the provisions of the General Data Protection Regulation, granted approval to carry out a sample check on pregnant women, on the status of vitamin D.

Application number of Request to collect data: 7380/27-5-2019

Approval Number/Date: Number 6 / June 6, 2019

Statement of informed consent

Informed consent was obtained from all individual participants included in the study

Funding

This research received no external funding.

Author Contributions

AK conceived the topic; AK, MD, AL and GI retrieved the literature; AK wrote the paper; KB collected the results of the values of 25(OH)D; MD, AL, EA and GI provided relevant methodological support and supervision. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

References

[1] Zu ZY, Jiang MD, Xu PP, Chen W, Ni QQ, Lu GM et al, Coronovirus disease 2019 (COVID-19): A perspective from China. Radiology. 2020; 296: E15-E25 https://pubmed.ncbi.nlm.nih.gov/32083985

[2] Nowson CA, McGrath JJ, Ebeling PR, Haikerwal A, Daly RM, Sanders KM et al, Vitamin D and health in adults in Australia and New Zeland: A position statement. Med J Aust. 2012; 196(11): 686-687 https://pubmed.ncbi.nlm.nih.gov/ 22708765

[3] Yu L, Ke HJ, Che D, Luo SL, Guo Y, Wu JL, Effect of Pandemic-Related Confinement on Vitamin D Status Among Children Aged 0-6 Years in Guangzhou, China: A cross-Sectional Study. Risk Manag Health Policy. 2020; 13: 2669-2675 https://pubmed.ncbi.nlm.nih.gov/ 33239928

[4] Wang G, Zhang Y, Zhao J, Zhang J, Jiang F, Mitigate the effects of home confinement on children during the COVID-19 outbreak. Lancet. 2020; 395(10228): 945-947 https://pubmed.ncbi.nlm.nih.gov/ 32145186

[5] Dominguez LJ, Farruggia M, Veronese N, Barbagallo M, Vitamin D sources, Metabolism, and Deficiency: Available Compounds and Guidelines for Its Treatment. Metabolites. 2021; 11(4): 255 https://pubmed.ncbi.nlm.nih.gov/33924215

[6] Cashman KD, Dowling KG, Skrabakova Z, Gonzalez-Gross M, Valtuena J et al, Vitamin D Deficiency in Europe: pandemic? Am J Clin Nutr. 2016; 103(4): 1033-1044 https://pubmed.ncbi.nlm.nih.gov/26864360

[7] Manios Y, Moschonis G, Lambrinou C, Tsoutsoulopoulou K, Binou P et al, A systematic review of vitamin D status in southern European countries. Eur J Nutr. 2018; 57(6): 2001–2036 https://pubmed.ncbi.nlm.nih.gov/29090332

[8] Holick MF, Vitamin D deficiency. N Engl J Med. 2007; 357(3): 266-281 https://pubmed.ncbi.nlm.nih.gov/17634462

[9] Bouillon R, Comparative analysis of nutritional guidelines for vitamin D. Nat Rev Endocrinol. 2017; 13(8): 466-479 https://pubmed.ncbi.nlm.nih.gov/28387318

[10] Papadakis G, Keramidas I, Kakava K, Pappa T, Villiotou V et al, Vitamin D and seasonal variation among Greek female patients with osteoporosis. In Vivo. 2015; 29(3): 409-413 https://pubmed.ncbi.nlm.nih.gov/25977390

[11] Hellenic National Meteorological Service/HNMS, Climatology. 2015; HNMS, Hellenic National Meteorological Service, https://www.emy.gr

[12] Hosseinpanah F, Pour SH, Heibatollahi M, Moghbel N, Asefzade S, Azizi F, The effects of air pollution on vitamin D status in healthy women: a cross sectional study. BMC Public Health. 2010; 10: 519 https://ncbi.nlm.nih.gov/20799984

[13] Heidari B, Mirghassemi MBH, Seasonal variations in serum vitamin D according to age and sex. Caspian J Intern Med. 2012; 3(4): 535-540 https://ncbi.nlm.nih.gov/24009930

[14] Haddad JG, Matsuoka LY, Hollis BW, Hu YZ, Wortsman, J, Human plasma transport of vitamin D after its endogenous synthesis. J Clin Invest. 1993; 91(6): 2552-2555 https://pubmed.ncbi.nlm.nih.gov/8390483

[15] Wacker M, Holick MF, Sunlight and Vitamin D: A global perspective for health, Dermatoendocrinol. 2013; 5(1): 51-108 https://pubmed.ncbi.nlm.nih.gov/24494042

[16] Motlagh AJ, Davoodvandi A & Saeieh SE, Association between vitamin D level in mother's serum and the level of vitamin D in the serum of pre-term infants. BMC Pediatrics. 2023, 23(97) https://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-023-03854-0

[17] Davis CD, Dwyer JT, The "sunshine vitamin": benefits beyond bone? J Natl Cancer Inst. 2007; 99(21): 1563-1565 https://pubmed.ncbi.nlm.nih.gov/17971523

[18] Dawodu A, Tsang RC, Maternal vitamin D status: effect on milk vitamin D content and vitamin D status of breastfeeding infants. Adv Nutr. 2012; 3(3): 353-361 https://pubmed.ncbi.nlm.nih.gov/22585912

[19] Picciano MF, Nutrient composition of human milk. Pediatr Clin North Am. 2001; 48(1): 53-67 https://pubmed.ncbi.nlm.nih.gov/11236733

[20] Khalaf M, The impact of Air Pollution on Health. Economy, Enviroment and Agricultural Sources. 2011; https://doi.org/10.5772/17838

[21] Kokkinari A, Dagla M, Lykeridou A, Bagianos K, Iatrakis G, How Did the COVID-19 Lockdown Affect Maternal Vitamin D (25(OH)D)Levels in Pregnant Women through Improved Air Quality? Environ Sci Proc. 2023; 26(1): 147 https://www.mdpi.com/2673-4931/26/1/147

[22] Surve S, Chauhan S, Amdekar Y, Joshi B, Vitamin D deficiency in Children: An update on its Prevalence, Therapeutics and Knowledge gaps. Indian J Nutri. 2017; 4(3): 167 https://opensciencepublications.com

[23] Misra M, Pacaud D, Petryk A, Collett-Solberg P, Kappy M, Vitamin D deficiency in children and its management: review of current Knowledge and recommendations. Pediatrics. 2008; 122(2): 398-417 https://pubmed.ncbi.nlm.nih.gov/18676559

[24] Braegger C, Campoy C, Colomb V, Decsi T, Domellof M et al, Vitamin D in the healthy European paediatric population. J Pediatr Gastroenterol Nutr. 2013; 56(6): 692-701 https://pubmed.ncbi.nlm.nih.gov/23708639

[25] Yu L, Ke HJ, Che D, Luo SL, Guo Y, Wu JL, Effect of Pandemic-Related Confinement on Vitamin D Status Among Children Aged 0-6 Years in Guangzhou, China: A cross-Sectional Study. Risk Manag Healthc Pol. 2020; 13: 2669-2675 https://pubmed.ncbi.nlm.nih.gov/33239928

[26] Kojima H, Takeda Y, Muromoto R, Takahashi M, Hirao T, Takeuchi S et al, Isoflavones Enhance Interleukin-17 Gene Expression via Retinoic Acid Receptor-Related Orphan Receptors α and γ. Toxicology. 2015; 329: 32-39 https://pubmed.ncbi.nlm.nih.gov/25583575