SARS-COV-2 MORBIDITY DEPENDING ON VITAMIN D STATUS

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BACKGROUND: The association between vitamin D deficiency and the severity of COVID-19 is currently being actively discussed around the world.

AIM: The aim of this study was to assess the prevalence of vitamin D insufficiency and deficiency and compare it with the incidence rates of SARS-CoV-2 in eight Federal Districts of the Russian Federation.

MATERIALS AND METHODS: We included 304,564 patients (234,716 women; 77,1%) with serum 25(OH)D levels results performed September 2019 through October 2020.

RESULTS: Only 112,877 people (37.1%) had a normal serum 25(OH)D level, others had a deficiency. Vitamin D insufficiency and deficiency was presented with the same frequency in women and men, and no differences were found depending on the geographical location and age in subjects from 18 to 74 years old. However, subjects over 75 years more often had vitamin D deficiency, while subjects under 18 years had normal levels in over 50% cases. In addition, 21,506 patients were tested for SARS-CoV-2 by PCR with further comparison of results with serum 25(OH)D level. The SARS-CoV-2 positivity rate was detected in 3,193 subjects, negative in 18,313. There were no differences in the morbidity in a vitamin D deficiency and a normal level. Thus, 14.8% subjects had positive PCR rates among vitamin D deficiency patients (4,978 tests), 14.9% when 25(OD)D level was from 20 to 30 ng/ml (7,542 tests), 15.0% among those who had 25(OH)D 30- 50 ng/ml (6,622 tests), and 13.9% when vitamin D was more than 50 ng/ml (4,612 tests).

CONCLUSION: There was no association between the COVID-19 incidence and vitamin D status in different regions of Russia. Although the nutrient deficiency persists in all regions and is most often diagnosed in people over 75 years old.

KEYWORDS: vitamin D deficiency; 25(OH)D; SARS-CoV-2; COVID-19; PCR rate.

ИНФИЦИРОВАННОСТЬ SARS-COV-2 В ЗАВИСИМОСТИ ОТ УРОВНЯ ОБЕСПЕЧЕННОСТИ ВИТАМИНОМ D

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ОБОСНОВАНИЕ. В настоящее время во всем мире активно обсуждается ассоциация между дефицитом витамина D и степенью тяжести течения COVID-19.

ЦЕЛЬ. Целью настоящей работы было оценить распространенность недостатка и дефицита витамина D и сопоставить с показателями инфицированности SARS-CoV-2 в восьми федеральных округах РФ.

МАТЕРИАЛЫ И МЕТОДЫ. В анализ включены результаты обследования 304 564 лиц (234 716 женщин; 77,1%), у которых были известны показатели концентрации 25(OH)D в сыворотке крови в период с сентября 2019 по октябрь 2020 г.

РЕЗУЛЬТАТЫ. Лишь 112 877 человек (37,1%) имели нормальный уровень 25(OH)D в сыворотке крови, остальные находились в недостатке или дефиците. Недостаток и дефицит витамина D были представлены с одинаковой частотой у женщин и мужчин, также не было выявлено различий в зависимости от географического расположения субъектов РФ и возраста у лиц от 18 до 74 лет. Однако лица старше 75 лет чаще имели дефицит витамина D, в то время как лица моложе 18 лет в более 50% случаев имели нормальный его уровень. У 21 506 больных было выполнено исследование на SARS-CoV-2 методом полимеразной цепной реакции (ПЦР), результаты которого сопоставлены с уровнем обеспеченности витамином D. Положительный результат ПЦР был выявлен у 3193 обследованных, отрицательный — у 18 313. Не выявлено различий в инфицированности пациентов в условиях дефицита и нормального уровня обеспеченности витамином D. Так, при уровне 25(OH)D ниже 20 нг/мл (4978 тестов) количество положительных ПЦР-тестов составило 14,8%, при уровне 20–30 нг/мл (7542 тестов) — 14,9%, 30–50 нг/мл (6622 тестов) — 15,0% и при значении более 50 нг/мл (4612 тестов) — 13,9%.

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ЗАКЛЮЧЕНИЕ. Таким образом, не выявлено зависимости между уровнем обеспеченности витамином D и числом положительных ПЦР-тестов к SARS-Co-2 ни в одном из регионов проживания, что свидетельствует об отсутствии связи между инфицированностью COVID-19 в РФ и уровнем обеспеченности витамином D, хотя дефицит нутриента сохраняется во всех регионах и наиболее часто диагностируется у лиц старше 75 лет.

КЛЮЧЕВЫЕ СЛОВА: дефицит витамина D; 25(OH)D; SARS-CoV-2; COVID-19; ПЦР-тест.

RELEVANCE

It is well-known that vitamin D deficiency is still a significant health-related social problem in many countries regardless of their geography [1–3]. Recent studies made in Russia have confirmed that vitamin D insufficiency and deficiency are widespread in Russia's northern and southern parts [4, 5]. Thus, according to the first-phase findings of a multi-centre study conducted in the spring 2020 in 10 regions of Russia, among the 445 examined patients (18–50) who had previously not consumed vitamin D supplements, whether as stand-alone medications or combined with calcium supplements, serum 25(OD) D level over 30 ng/mL was found in only 15.73% of patients, whereas vitamin D insufficiency or deficiency was diagnosed in 84.27% [5]. As we compare our findings with those of earlier studies [4], it is notable that vitamin D insufficiency and deficiency are still widespread in Russia's population, whereas the share of those with normal vitamin D status does not exceed 20%. Considering well-known pleiotropic effects of vitamin D, its potential contribution to the prevention and treatment of acute respiratory diseases, including COVID-19 infection, is currently widely discussed [6–9].

In the literature existing as on 1 May 2021, we identified over 90 articles and surveys on the topic of correlation between low 25(OD) D blood content and COVID-19 incidence, severity and outcome [10]. It ought to be said that most of these publications are descriptive surveys and meta-analyses. A very small part of the studies is represented by original research featuring primary data.

Contemporary literature presents data indicating so called immunomodulatory effects of vitamin D [11, 12]. Thus, its active role in both cell immunity and antibody response is confirmed [13–15]. Published analysis demonstrates higher frequency of positive PCR tests for SARS-CoV-2 in patients with vitamin D deficiency than in those with normal 25(OD) D level, *i.e.*, over 30 ng/mL [16]. Moreover, data suggest that COVID-19 course tends to be milder in those with higher 25(OD) D blood content and hospital stay tends to be shorter if patients are given vitamin D supplements [17, 18]. To date, Russian research on this topic has been rather scarce, hence our interest therein.

PURPOSE

Verify the prevalence of vitamin D insufficiency and deficiency and cross reference these data against SARS-CoV-2 incidence in patients with various vitamin D status residing in different federal districts of Russia.

MATERIALS AND METHODS

Research Place and Time

Research venue. Almazov National Medical Research Centre, St Petersburg, Russia.

Research time. September 2019 – October 2020. Statistical data processing was conducted between 1 February 2021 and 31 May 2021.

Population size values were determined based on data of the Federal State Statistics Service of Russia as on 1 February 2020 [19]; COVID-19 cases and mortality values were determined as per the Ministry of Health data [20]. Data presented in this article were verified as on 25 February 2021.

Examined population

Population. Serum 25(OD) D tests were made in 304,564 patients residing in eight federal districts of Russia. These patients turned to HELIX LLC for tests; 234,716 of them (77.1%) were females. Test findings were cross referenced against these patients' PCR tests for SARS-CoV-2/SARS-CoV.

Criteria for inclusion. Males and females 18 and over turning for serum 25(OD) D tests to HELIX LLC from September 2019 to October 2020.

Criteria for exclusion. None.

Method of examined population(s) sampling

Out from HELIX LLC database, we selected serum 25(OD) D test results for patients who had at least one serum 25(OD) D test from September 2019 to October 2020. In addition, out of these 304,564 patients we selected 32,197 who had at least one PCR test for SARS-CoV-2 within the same period. If at least one PCR test was positive (+), such patient was considered to have contracted SARS-CoV-2. If a patient had several serum 25(OD) D tests, we used the reading obtained most closely to the date of their PCR test.

Research design

This research was made as a case–control study. Patient data were provided by HELIX LLC in depersonalised form.

Methods

Chemiluminescence analysis was used to determine 25(OD) D level. UniCel DxI800 analysers (Beckman Coulter, USA) and UniCel DxI systems were used. As per Russian Endocrinologists Association guidelines, vitamin D status was considered normal if serum 25(OD) D level was at or above 30 ng/mL (at or above 75 nmol/L); a patient was deemed to have vitamin D insufficiency if their serum 25(OD) D level was at or above 20 ng/mL but below 30 ng/mL (at or above 50 nmol/L but below 75 nmol/L); deficiency if the readings were under 20 ng/mL (50 nmol/L) and acute deficiency if the readings were under 10 ng/mL (25 nmol/L). The range of 25(OD) D measurements was 4.4 to 210.0 ng/mL.

SARS-CoV-2 RNA detection was conducted through reverse transcription and real-time PCR (SARS-CoV-2/SARS-CoV) as per TU 21.20.23-116-46482062-2020 standard with DT Prime detection amplifier (DNA Technology LLC) and coronavirus RNA detection kits (DNA Technology TS LLC).

Statistical analysis

Statistical data analysis was performed with IBM SPSS Statistics for Windows ver. 26 (IBM Corp., Armonk, N.Y., USA).

Ethical review

Research protocol ver. 1.1 dated 23 October 2020 was approved by Almazov National Medical Research Centre's internal Ethics Committee on 30 November 2020 (extract no. 1011-20-02C).

FINDINGS

Among a total of 304,564 patients tested by HELIX LLC between September 2019 and October 2020 who had serum 25(OD) D level test results, there were 45,811 patients under 18 (15.0%); in this group, 23,617 (51.6%) were females. The 18–44 group was much more numerous: 154,310 (50,7%); in this group, 126,076 were females (81.7%). The 45–60 group had 62,853 patients (20.6%); in this group, 50,635 were females (80.6%). The 61–74 group had 34,331 patients (11.3%); in this group, 28,576 were females (83.2%). The over 75 group had 7,259 patients (2.4%); in this group, 5,812 were females (80.1%). We found that, regardless of the age, most of those turning for a serum 25(OD) D test were females. Vitamin D deficiency was diagnosed in 88,427 out of 304,564 patients (29.0%) and vitamin D deficiency in 103,260 patients (33.9%). Thus, despite a vigorous awareness campaign launched in Russia five years ago to promote prevention activities against vitamin D insufficiency and deficiency, only 112,877 patients (37.1%) had normal serum 25(OD) D level. The rest had either vitamin D insufficiency or deficiency.

Statistical analysis showed that the frequency of vitamin D deficiency was the same in females and males, *i.e.*, 29.5% and 27.5%, respectively (p>0.05). Similar results were obtained regarding vitamin D insufficiency: its frequency in females and males was 34.0% and 33.6%, respectively (p>0.05). Thus, we did not find any gender-specific variance as to the frequency of vitamin D insufficiency and deficiency from September 2019 to October 2020.

As for the patients' age, we found that in the under 18 group vitamin D deficiency was diagnosed in 22.3% of patients and vitamin D insufficiency in 31.9% of patients. In the 18–44 group, these values were 29.2% and 34.1%, respectively; in the 45–60 group, 30.0% and 35.2%, respectively, and in the 61–74 group, 32.6% and 34.8%, respectively. In the over 75 group, vitamin D deficiency and insufficiency were diagnosed in 42.2% and 27.2% of patients, respectively. Thus, we found no age-specific variance as to the frequency of vitamin D insufficiency and deficiency in patients 18–74. However, almost half of under 18 patients had a normal 25(OD) D level, whereas for those over 75 vitamin D deficiency was relatively more frequent (see Figure 1).

It must be said that both among those with normal 25(OD) D blood level and those with low levels there were probably some who were consuming vitamin D supplements; however, within this study the ratio of such patients in the total examined population could not be determined.

As to the correlation between the patients' place of residence and 25(OD) D blood level, we found that among the 121 examined residents of the Far Eastern Federal District, 62 (51.2%) were diagnosed with vitamin D insufficiency or deficiency; among the 23,894 residents of the Volga Federal District, 14,378 (60.2%) were so diagnosed; among the 95,147 residents of the Northwestern Federal District, 58,566 were so diagnosed; among the 10,948 residents of the Siberian Federal District, 6,466 (59.1%) were so diagnosed; among the 43,482 residents of the Ural Federal District, 28,246 (65.0%) were so diagnosed; among the 60,518 residents of the Central Federal District, 37,822 (62.5%) were so diagnosed; among the 70,454 residents of the Southern Federal District, 46,147 (66.5%) were so diagnosed; and among the 1,394 residents of the North Caucasian Federal District, 921 (66.1%) were so diagnosed. Thus, almost every federal district had over 60% of examined patients diagnosed with either vitamin D insufficiency or deficiency. These figures were slightly lower than those obtained by previous research. However, given the fact that even patients consuming vitamin D supplements could be diagnosed with vitamin D insufficiency or deficiency, our data tell that the majority of patients we examined did not have target 25(OD) D blood levels, regardless of their place of residence (see Figure 2).

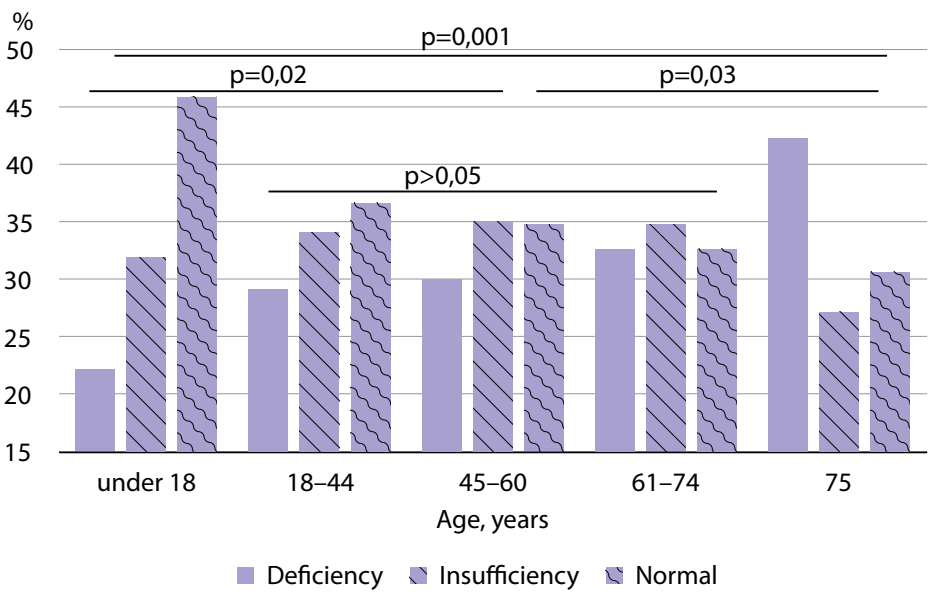

Figure 1. Prevalence of vitamin D deficiency by age

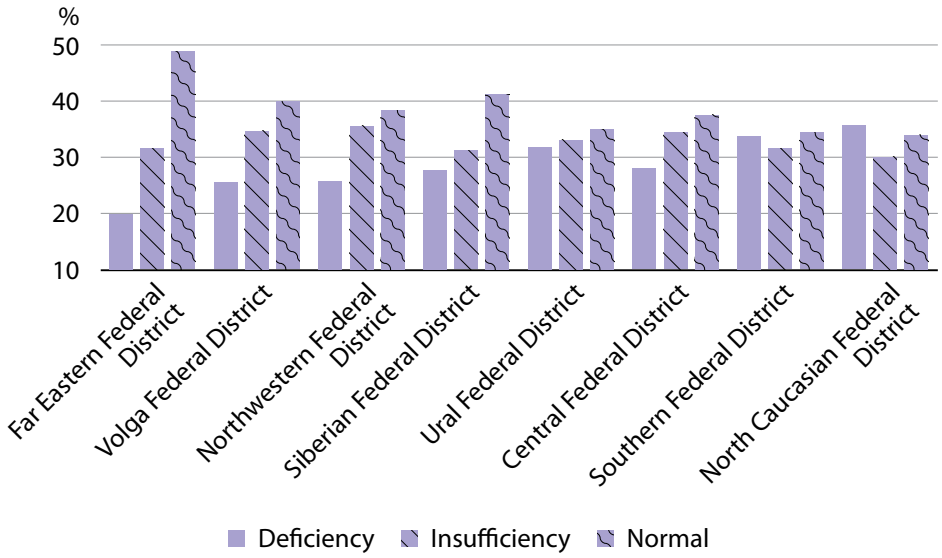

Figure 2. Prevalence of vitamin D deficiency by federal district

From among the 304,564 patients who had results of serum 25(OD) D tests, 32,197 made PCR tests for SARS-CoV-2 between 26 March 2020 and 31 October 2020 and had their PCR test results available. Having eliminated some patients' repeat tests, we were left with 21,506 test results available for statistical analysis. Among them, 3,193 had at least one positive PCR test; 18,313 tests were negative. These PCR test results were cross referenced against data on vitamin D status of various regions' residents. If a patient had several serum 25(OD) D tests, we used the reading obtained most closely to the date of their PCR test.

Patients who had positive PCR tests demonstrated similar frequency of serum 25(OD) D levels and similar prevalence of vitamin D insufficiency and deficiency to those of PCR-negative patients (see Table 1).

As part of this study, we also analysed the Federal State Statistics Service's data on population size and the Ministry of Health's statistics on COVID-19 cases and mortality. We found that, as on 25 February 2021, the number of COVID-19 cases was slightly higher in the Northwestern and Central federal districts, whereas COVID-19 mortality rate ranged from 1.3% (in Far Eastern Federal District) to 3.2% (Southern Federal District) (see Table 2).

Based on available data on population size, COVID-19 cases and mortality, we calculated COVID-19 infections and mortality rates in various federal districts of Russia as on 25 February 2021 (see Table 2, Figure 3).

The above data show that the highest number of COVID-19 cases was found in the Northwestern and Central federal districts, whereas COVID-19 mortality rate was slightly higher in the Siberian and Southern federal districts.

Our analysis found no correlation between the rate of positive PCR tests and serum 25(OH)D levels, *i.e.*, vitamin D status. Thus, in patients with serum 25(OH)D under 20 ng/mL (vitamin D deficiency), 4,978 PCR tests were made, out of which 14.8% were positive. In patients with serum 25(OH)D between 20 ng/mL and 30 ng/mL, 7,542 PCR tests were made, out of which 14.9% were positive. In patients with serum 25(OH)D between 30 ng/mL and 50 ng/mL, 6,622 PCR tests were made, out of which 15.0% were positive. In patients with serum 25(OH)D over 50 ng/mL, 4,612 PCR tests were made, out of which 13.9% were positive.

Table 1. 25(OD) D levels and frequency of vitamin D deficiency in patients with positive PCR test for SARS-CoV-2

Parameter	Everyone n=21,506	PCR (+) n=3,193	PCR (-) n=18,313	p
25(OH)D, ng/mL				
Min	3.22	4.24	3.22	
Max	210.5	159.52	210.5	
Average ± SD	31.24 ± 16.69	30.96 ± 16.35	31.29 ± 16.75	>0.05
Median, Me	27.41	27.29	27.43	
[Q25; Q75]	[20.54; 37.3]	[20.49; 36.68]	[20.55; 37.41]	
Vitamin D status				
Normal, n (%)	8,988 (41.8)	1,337 (41.9)	7,651 (41.8)	
Insufficiency, n (%)	7,542 (35.1)	1,120 (35.0)	6,422 (35.0)	>0.05
Deficiency, n (%)	4,976 (23.1)	736 (23.1)	4,240 (23.2)	
including acute deficiency (<10 ng/mL), n(%)	356 (1.7)	45 (1.4)	311 (1.7)	

Table 2. COVID-19 cases and mortality by federal district (data shown as on 25 February 2021)

Federal district	Population size (Federal Statistics Service)	COVID-19 cases n	COVID-19 infections per 1,000 population	COVID-19 mortality	Mortality rate (%)
Far Eastern	8,131,555	253,091	31.12	3,261	1.3
Volga	29,087,997	518,761	17.83	10,231	2.0
Northwestern	13,952,964	704,649	50.50	15,363	2.2
Siberian	17,009,249	349,461	20.55	10,180	2.9
Ural	12,333,234	262,701	21.30	4,986	1.9
Central	39,251,953	1,661,777	42.34	28,868	1.7
Southern	16,498,642	255,573	15.49	8,081	3.2
North Caucasian	9,967,301	163,043	16.36	3,435	2.1
TOTAL	146,232,895	4,169,056	28.51	80,970	1.9

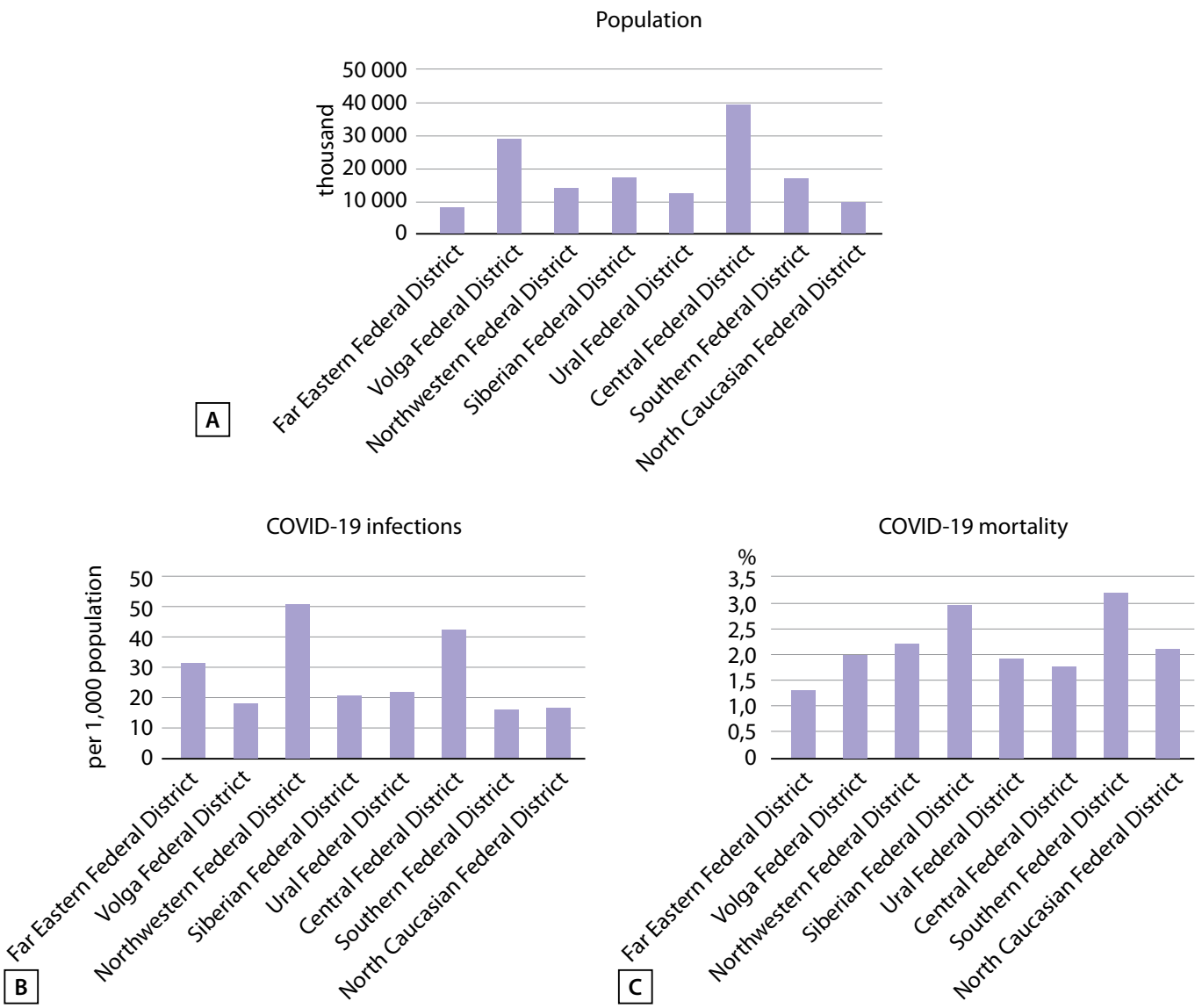

Figure 3. Population size data (A), COVID-19 infections (B) and COVID-19 mortality (C) as on 25 February 2021, adapted from the Ministry of Health website data

Table 3. Distribution of examined patients by vitamin D status and PCR test results, by federal district

Federal district	PCR (+) n=3,193	Vitamin D status			PCR (-) n=18,313	Vitamin D status		
		Normal n=1,337	Insufficiency n=1,120	Deficiency n=736		Normal n=7,651	Insufficiency n=6,422	Deficiency n=4,240
Far Eastern, n (%)	2 (16.7)	1 (50.0)	1 (50.0)	0	12 (85.7)	4 (33.3)	4 (33.3)	4 (33.3)
Volga, n (%)	81 (24.1)	39 (48.1)	30 (37.0)	12 (14.8)	336 (80.6)	167 (49.7)	98 (29.2)	71 (21.1)
Northwestern, n (%)	1,677 (15.7)	716 (42.7)	607 (36.2)	354 (21.1)	10,713 (86.5)	4,411 (41.2)	3,857 (36.0)	2,445 (22.8)
Siberian, n (%)	74 (30.2)	38 (51.4)	23 (31.1)	13 (17.6)	245 (76.8)	119 (48.6)	75 (30.6)	51 (20.8)
Ural, n (%)	602 (20.8)	236 (39.2)	222 (36.9)	144 (23.9)	2,897 (82.8)	1,150 (39.7)	1,045 (36.1)	702 (24.2)
Central, n (%)	360 (13.8)	165 (45.8)	113 (31.4)	82 (22.8)	2,610 (87.9)	1,231 (47.2)	835 (32.0)	544 (20.8)
Southern, n (%)	102 (25.4)	43 (42.2)	39 (38.2)	20 (19.6)	401 (79.7)	169 (42.1)	171 (42.6)	61 (15.2)
North Caucasian, n (%)	295 (26.8)	99 (33.6)	85 (28.8)	111 (37.6)	1,099 (78.8)	400 (36.4)	337 (30.7)	362 (32.9)

We also analysed the rate of positive PCR tests (%) by federal district and vitamin D status. The Far Eastern Federal District was excluded from this analysis due to small sample size; no reliable variance was found between the other federal districts (see Table 3).

The above data show that 33.6% to 51.4% of PCR-positive patients had normal vitamin D status (over 30 ng/mL), whereas the respective ratio among PCR-negative patients was 36.4% to 48.6%. Somewhat unusual is the North Caucasian Federal District, in which the ratio of PCR-positive patients with vitamin D deficiency was highest (37.6%). However, the same prevalence of vitamin D deficiency was observed in PCR-negative patients, too. A more detailed analysis found no correlation between COVID-19 cases and serum 25(OH)D level, either (see Figure 4).

Thus, our findings once again confirmed high prevalence of vitamin D insufficiency and deficiency in the population of various regions of Russia and established no correlation between COVID-19 cases and vitamin D status, whether in Russia's northern, central, or southern parts.

DISCUSSION

Sample representativeness

SARS-CoV-2-induced COVID-19 pandemic is a major health-related social problem first encountered by humankind in the last year [21, 22]. It is well-known that most of COVID-19 patients recover; however, in some of them this infection may cause severe system damage requiring hospitalisation and quite often be quite lethal [23]. At present, medical science knows several factors causing severe COVID-19 course and lethal outcome, such as advanced age, male sex, sugar diabetes and/or obesity, and cardiovascular diseases [22, 24]. In addition to these, recent years' studies have shown that low vitamin D status may be a modifiable risk factor for COVID-19 course that negatively affects both the course and the outcome of the disease [25, 26]. The number of ARVI patients and persons with low vitamin D increases as one moves from south to north [27]; this observation and the fact that the cells of human immune system contain vitamin D receptors and

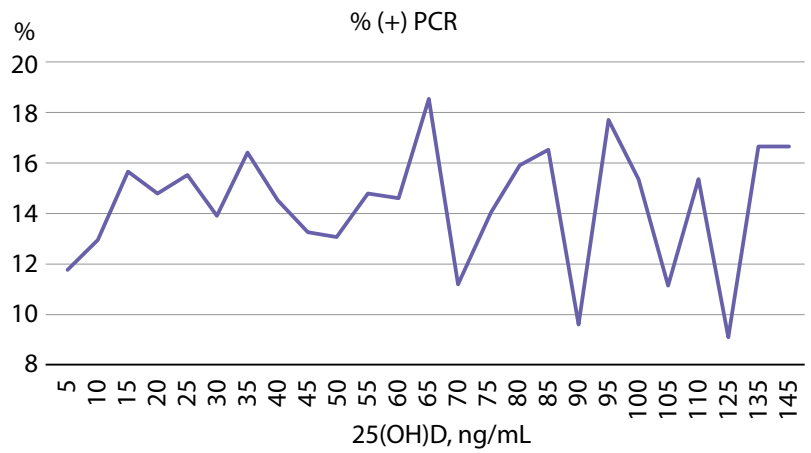

Figure 4. Ratios of positive PCR tests with various serum 25(OH)D levels

express 1A hydroxylase that contributes to the formation of active D hormone (calcitriol) have triggered studies in vitamin D immunomodulatory effects [11, 12]. The first data on 25(OH)D levels in COVID-19 patients came from China; the relevant studies described an association between low vitamin D status and COVID-19 course severity/outcome [28, 29]. Subsequent research affirmed an inverse relationship between serum 25(OH)D levels and COVID-19 course severity and mortality [30, 32].

To date, the largest study combining data on PCR tests for SARS-CoV-2 and vitamin D status in over 190,000 patients has been conducted in the USA. Its findings suggest that the number of positive PCR tests depends on serum 25(OH)D level [16]. Thus, the authors established that with 25(OH)D level under 20 ng/mL 39,120 patients (12.5%) had positive PCR tests for SARS-CoV-2 (95% Confidence Interval 12.2%–12.8%). 25(OH)D concentrations between 30 ng/mL and 34 ng/mL were associated with slightly lower numbers of COVID-19 infections: 27,870 or 8.1% (95% Confidence Interval 7.8%–8.4%). Finally, with 25(OH)D levels over 55 ng/mL only 12,321 patients (5.9%) had positive PCR tests (95% Confidence Interval 5.5%–6.4%). Thus, the authors demonstrated that the highest numbers of COVID-19 infections occurred with blood 25(OH)D levels under 20 ng/mL, whereas the ratio of positive PCR tests for SARS-CoV-2 in patients with over 50 ng/mL was 40% lower than that in patients with vitamin D deficiency.

Matching our findings against those of other studies

In contrast with the overseas study, both our findings and those of previous Russian research [4, 33] do not establish any consistent pattern of frequency of vitamin D insufficiency and deficiency depending on the region's geography. Instead, they show equally low 25(OH)D levels across all federal districts in which patients were examined. However, our data do show that southern regions of Russia (the Southern, Volga, Far Eastern and North Caucasian federal districts) have slightly higher ratios of patients with vitamin D deficiency than do central regions (the Northwestern and Siberian federal districts), which is probably due to better awareness and more frequent prescriptions of colecalciferol in preventive doses in relatively northern regions. At the same time, we found that vitamin D deficiency is more frequent in patients over 75, whereas normal vitamin D status is typical for half of those under 18, which concurs with the findings of previous research [1, 3]. However, insufficiency of data on consumption of vitamin D supplements prevented us from assessing the relationship between colecalciferol administration and vitamin D status.

Practical significance of the findings

Analysis of data on COVID-19 cases in residents of eight federal districts based on results of PCR tests made by a major laboratory chain (HELIX LLC) showed no variance between the ratios of positive tests for SARS-Co-2 across all regions. Due to a small number of positive PCR tests in residents of the Far Eastern Federal District whose vitamin D status was known by 31 October 2020, we cannot reliably assess the contribution of vitamin D deficiency to COVID-19 infections in Russia's Far East. However, based on data for other regions, including southern ones, we did not find any correlation between 25(OH)D blood levels and the ratio of positive PCR tests for SARS-CoV-2. Thus, in contrast to data published by H.W. Kaufman *et al.*, prevalence of COVID-19 infections in Russia is not associated with vitamin D status, although vitamin D deficiency is prevalent across all regions of Russia and in more frequent in patients over 75. Given the risk factors for COVID-19 course, we believe it is highly important to focus more strongly on matters of prevention and treatment, especially with that age group.

Limitations of our study

Insufficiency of information on the facts, dosage and duration of vitamin D supplements administration. Insufficiency of data on diseases, including gastrointestinal tract pathologies and kidney pathologies which could have affected the 25(OH)D levels in the examined group.

Areas of further research

Plans for further research include interventional studies seeking to assess the contribution of treatment with standard and saturating colecalciferol doses to SARS-CoV-2 prevention among medical staff of COVID-19 wards and to reduction of COVID-19 course severity and mortality, in addition to the standard treatment.

CONCLUSION

Thus, our findings once again confirm high prevalence of vitamin D deficiency in Russia, which has persisted during the COVID-19 pandemic and is more frequent in the over 75 group. However, we did not find any correlation between vitamin D status and the ratio of positive OCR tests for SARS-CoV-2 in any of Russia's regions.

ADDITIONAL INFORMATION

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