AGE-RELATED ISSUES OF VITAMIN D DEFICIENCY AND COVID-RELATED HEALTH OUTCOMES IN GEORGIA

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SUMMARY

Background: In patients hospitalized for COVID-19, vitamin D deficiency was highly prevalent. Elderly patients who survived COVID-19 took more time for a full recovery compared to other age groups.

Objective: This study aims to evaluate the age peculiarities of vitamin D deficiency and COVID-related health outcomes (hospitalization, transfer to ICU unit, requirement of oxygen therapy, and treatment by glucocorticoids).

Materials and Methods: Presented retrospective cross-section study was performed based on National Center of Disease control and Public Health (NCDC) data of Georgia. After obtaining the written informed consent form, 384 persons from the NCDC database were included in the study group. Study subjects were divided into two age groups: group 1 – patients aged 50 years – n=156; and Group 2 – patients aged < 50 years – n=228.

Results: The Mean serum 25(OH)D levels in the study groups did not differ significantly. However, these values were significantly lower in hospitalized patients of both groups. The odds of hospitalization and the requirement of oxygen therapy in group 1 were significantly higher compared to group 2 (OR = 3.79, p<0.001; OR = 5.10, p=0.002, respectively). The odds of the requirement of transfer to the ICU unit (OR = 2.22, p=0.387) and glucocorticoid treatment (OR = 2.73, p=0.077) between the groups were insignificant.

Conclusion: Our study revealed significantly worse COVID-19-related health outcomes in elderly patients than in younger age groups. However, the difference between groups in mean levels of serum 25-hydroxyvitamin D [25(OH)D] in hospitalized patients was not statistically significant.

Keywords: COVID-19; elderly; health outcomes; hospitalization; vitamin D.

INTRODUCTION

The COVID-19 pandemic was the outbreak following SARS in 2002 and MERS infections in 2012.[1,2] However, in contrast to previous ones, COVID-19 has higher transmission rates. It thus incurs more challenges in terms of prevention and treatment.[2] Mortality and other complications were the most susceptible adverse outcomes from COVID-19.[3] Their risk also increases in the presence of multiple comorbidities such as diabetes, cardiovascular disease, respiratory disease, malignancy and obesity.[3-6]

SARS-CoV-2 infection induces local and systemic inflammatory responses in humans.[7] Inflammation accompanied by an exaggerated immune response leads to pyroptosis and tissue damage in patients with COVID-19.[8] When SARS-CoV-2 infects the lungs, it causes alveolar epithelial cell death, endothelial disruption, increased lung permeability, and alveolar edema. It can lead to acute respiratory distress syndrome (ARDS) and multiorgan failure.[9]

In patients hospitalized for COVID-19, vitamin D deficiency was highly prevalent.[10] Therefore, it is rational to assume a beneficial role of vitamin D supplementation in preventing, reducing symptoms, or improving the prognosis of this disease. Several dozen studies have been conducted to determine the effect of vitamin D on COVID-19. Among them, a few have found promising results. An RCT of oral vitamin D3 (cholecalciferol; 60,000 IU daily), with a therapeutic target of serum 25(OH) D > 50 ng/mL, was found to significantly induce negative conversion of SARS-CoV-2-RNA and lead to a decrease in fibrinogen levels.[11] Other small-scale studies have also shown that vitamin D supplementation during or in the month preceding SARS-CoV-2 infections was associated with less severe outcomes, including lower mortality, even in elderly patients.[12] Asymptomatic or mildly symptomatic patients with COVID-19 given vitamin D showed improvement in related symptoms on day 14 but did not significantly reduce the time to negative transformation of SARS-CoV-2 RNA virus.[13] Another study found that a single high dose (200,000 IU) of vitamin D did not reduce the length of hospital delay or mortality in patients hospitalized for moderate to severe COVID-19.[14] Elderly patients survived after COVID-19 took more time for the full recovery compared to other age groups. The outcome of these conditions was rapid loss of muscle mass after hospital discharge due to immobilization, which can increase the risk of frailty, falls, fractures, and mortality.[15]

Therefore, our study aimed to investigate the age peculiarities of vitamin D deficiency and COVID-related health outcomes (hospitalization, transfer to ICU unit, requirement of oxygen therapy, and treatment by glucocorticoids).

METHODS

Study Design and Subjects

The presented retrospective cross-section study was performed based on the data of the National Center for Disease Control and Public Health (NCDC) of Georgia. 475 records of patients with determined serum 25-hydroxyvitamin D [25(OH)D] levels were randomly selected for the study. Researchers visited these patients, and after obtaining written informed consent, 384 persons from the NCDC database were included in the study group.

Study Parameters

The data on hospitalization, duration, transfer to the ICU unit, oxygen therapy requirement, glucocorticoid treatment, and symptoms were extracted from the NCDC database. The patients were

surveyed using particular structured questionnaires to provide information about the presence of vitamin D supplementation before the SARS-virus confirmation.

Study Groups

Study subjects were divided into two age groups: group 1 – patients aged 50 years – n=156; and Group 2 – patients aged < 50 years – n=228.

Statistical Analysis

The study results were statistically analyzed using SPSS 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean and standard deviation (SD), and differences were assessed by analysis of variance. Categorical variables were compared using Pearson's chi-square or Fisher's exact tests. Odds ratios (ORs) and 95% CIs within the presented study were estimated. P values of <0.05 were considered as statistically significant.

RESULTS

Study Characteristics

Table 1 gives the age, body mass index (BMI) data, and distribution by gender and body weight status of the patients in the study groups.

Table 1. *Age, BMI, and the distribution of patients by gender and body weight status in the study groups.*

#	Parameter	Group 1 (n=156)		Group 2 (n=228)	
		Mean	SD	**Mean**	SD
1	**Age, years**	**63.9**	7.9	**27.9**	10.4
2	**BMI, kg/m²**	**28.1**	9.0	**24.8**	4.0
3	**Body Weight Status**	**n=**	%	**n=**	%
	Normal	**32**	20.5%	**123**	53.9%
	Overweight	**91**	58.3%	**81**	35.5%
	Obesity	**33**	21.2%	**24**	10.5%
4	**Gender**	**n=**	%	**n=**	%
	Males	**33**	21.2%	**60**	26.3%
	Females	**123**	78.8%	**168**	73.7%

It is clear from the table that age did not differ between groups significantly. No significant difference was found between the groups according to the distribution by the age groups (chi2-test = 1.706, df=2, p=0.426). BMI mean values differed significantly between the groups (p<0.05). The same trend was found in the distribution by body mass between the groups – chi2-test = 43.36, df=2, p<0.001. Gender distribution was not significantly different.

Chart 1 shows the mean levels of serum 25(OH)D in the study groups. The difference between these values was not significant — t=0.695, p=0.487.

Chart 1. *Mean levels of serum 25-hydroxyvitamin D [25(OH)D]*

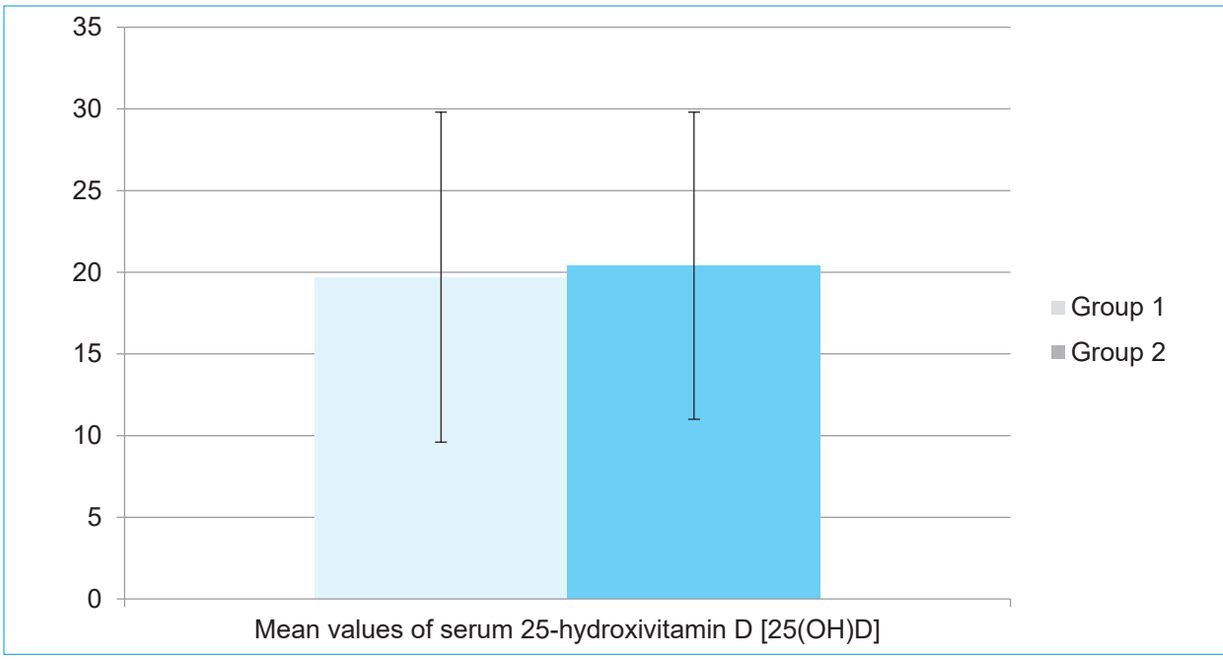


Table 2 gives the data on hospitalization rates, transfer to the ICU unit, oxygen therapy requirements, glucocorticoid treatment, and SARS-COV-2 infection symptoms extracted from the NCDC database.

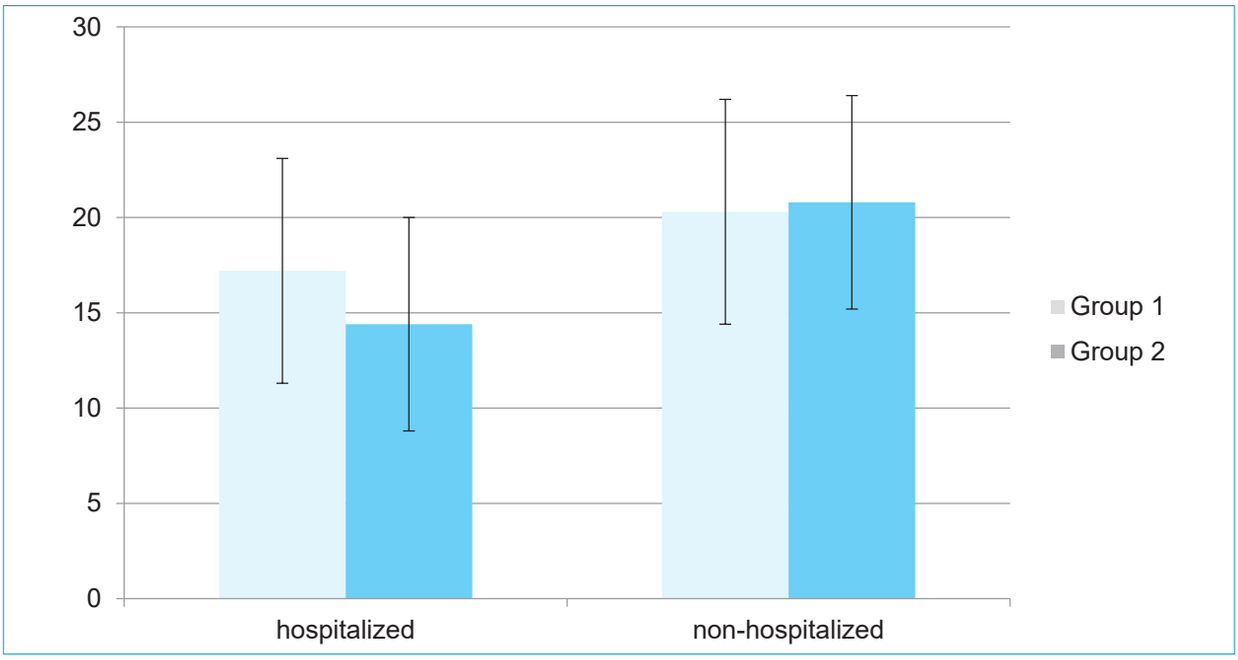
Table 2. *The distribution of patients by the hospitalization rates, transfer to the ICU unit, the requirement of oxygen therapy, the treatment by glucocorticoids, and SARS-infection symptoms in the study groups*

#	Health outcomes	Group 1 (n=156)		Group 2 (n=228)	
		n=	%	n=	%
1	Hospitalization	**31**	19.9%	**14**	6.1%
2	Transfer to ICU unit	**3**	1.9%	**2**	0.9%
3	Requirement of oxygen therapy	**16**	10.3%	**5**	2.2%
4	Treatment by glucocorticoids	**9**	5.8%	**5**	2.2%

The odds of hospitalization and the requirement of oxygen therapy in group 1 were significantly higher compared to group 2 (OR = 3.79, 95%CI 1.94 – 7.40, F-test = 3.91, p<0.001; OR = 5.10, 95%CI 1.83 – 14.22, F-test = 3.11, p=0.002, respectively).

The odds of the requirement of transfer to the ICU unit (OR = 2.22, 95%CI 0.37 – 3.42, F-test = 0.87, p=0.387) and the treatment by glucocorticoids (OR = 2.73, 95%CI 0.90 – 8.31, F-test = 1.77, p=0.077) between the groups were not significant.

Chart 2. *Mean levels of serum 25-hydroxyvitamin D [25(OH)D] in hospitalized and non-hospitalized patients in both groups.*



Mean levels of serum 25-hydroxyvitamin D [25(OH)D] in hospitalized patients were significantly lower in both groups compared to non-hospitalized patients ($p<0.05$). However, the difference in these levels between groups of hospitalized patients was insignificant ($p>0.05$).

DISCUSSION

There has been much discussion about the impact of vitamin D on SARS-COV-2 infection. Vitamin D may alter the disease manifestations depending on its influence on macrophage function and innate immunity. Vitamin D supplementation becomes relevant in the absence of highly effective prevention and treatment strategies for the pandemic. Considering the drugs' availability and very economical pricing, especially in developing countries (countries of Group A and B by Research4Life program16), vitamin D supplementation should be an important option for the populations at risk.

Previous systematic reviews have clearly shown an inverse association between 25(OH)D concentration and acute respiratory tract infections8,17, but these studies were not directly focused on SARS-CoV-2 infection. Similar to our findings, a study from the UK by Panagiotou et al. found that low serum 25(OH)D levels in 134 hospitalized patients with COVID-19 were associated with a more severe disease course.[18]

Conversely, a study using the UK Biobank looked at 348 598 participants, of whom only 449 had a confirmed diagnosis of COVID-19 as defined by a positive laboratory test for SARS-CoV-2 (only 0.13% of the study population), and they did not find any association between 25(OH)D and risk of COVID-19 infection.[19] In addition to the low number of patients with COVID-19, other weaknesses in this study included heterogeneity in severity and management of COVID-19 cases (likely a mixture of inpatient and community, instead of focusing on COVID-19 cases in only one

setting), serum 25(OH)D measurement between 2006 and 2010, and not contemporaneously with COVID-19 infection 10 to 14 years after recruitment to the UK Biobank, and no mention of validation of 25(OH)D measurement.

In terms of 25(OH)D and COVID-19 disease severity, a study from India of 154 patients admitted to hospital with COVID-19 reported that the mean 25(OH)D level was <30 ng/mL (insufficient range), and patients admitted to the intensive care unit and those that died from COVID-19 were more deficient in vitamin D than survivors.[20] Another study from Belgium (n = 186) reported similar findings of greater deficiency rates in patients with more severe disease.[21] Similarly, a study from Switzerland demonstrated that 25(OH)D concentrations were significantly lower in patients with COVID-19 than in those without the disease.[22]

Other studies have also demonstrated a correlation between vitamin D deficiency and COVID-19 infection, contrary to the study using patients from the UK Biobank. A study from Israel with 7807 subjects demonstrated that 25(OH)D concentrations were significantly lower among those who tested positive for COVID-19 than those who were COVID-19 negative.[23] A study from Wuhan, China, showed in a multivariable logistic regression that vitamin D deficiency (<30 nmol/L) was significantly associated with COVID-19 severity.[24]

It has long been clear that groups that traditionally exhibit vitamin D deficiency or insufficiency, such as older adults and nursing home residents and Black, Asian, and minority ethnic populations, are the same groups that COVID-19 has disproportionately impacted. Additionally, increased time spent indoors due to strict lockdowns and shielding triggered concerns that some people might not obtain the necessary physiological levels of vitamin D from sunlight.[25]

CONCLUSION

Our study revealed significantly worse COVID-19-related health outcomes in elderly patients compared to the younger age group. However, the difference between groups of mean levels of serum 25-hydroxyvitamin D [25(OH)D] in hospitalized patients was not statistically significant.

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Conflict of Interest:

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