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The relationship between vitamin D deficiency and mortality in older adults before and during COVID-19 pandemic

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ABSTRACT

Background: Vitamin D is an essential fat-soluble vitamin thought to be associated with chronic diseases, mortality and COVID-19.
Objective: To investigate the association between 25(OH) vitamin D levels and mortality of chronic diseases in subjects aged ≥65 years before and during COVID-19 pandemic.
Methods: A single-center, retrospective study was performed using the hospital database of subjects aged 65 years and older who had undergone vitamin D measurement between 01.01.2019 and 31.12.2021. All patients with vitamin D measurement (N = 2155) were followed as a cohort from the date of serum vitamin D analysis through death date or 01.01.2022. Age, gender, chronic diseases, survival status, date of death of the deceased, laboratory values including complete blood count, liver/renal functions and 25(OH) vitamin D levels were all noted. Subjects were classified into three groups according to their 25(OH) vitamin D levels; severe deficient group (<10 ng/ml), moderate deficient group (10–19.9 ng/ml), and control group (≥20 ng/ml).
Results: Data of 1949 subjects were included in this retrospective analysis and 206 of them (10.6%) had at least two vitamin D measurements. Until the time of data collection (01.01.2022), 94 of the cases had died within the last three years, and only five of them had repeated measurements. While the mean vitamin D level was lower, age and frequency of dyslipidemia, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), arrhythmia, dementia and severe vitamin D deficiency (<10 ng/ml) were higher in subjectswho died (all p<0.05). According to the Cox proportional hazards model; age, presence of CAD, COPD, arrhythmia, dementia, anemia and severe vitamin D deficiency were independently related with mortality (all p<0.05). After adjusted by age, gender, and comorbidities, the probability of death was found to be 1.91 (95% CI=1.12–3.24) times higher in the severe vitamin D deficient group.
Conclusions: The results of this study have shown that - after having adjusted for potential factors - severe vitamin D deficiency (<10 ng/ml) seems to be an independent predictor for non-cancer mortality. Although vitamin D measurement/treatment is very easy and cheap where, on the contrary, severe vitamin D deficiency can be quite mortal.

Introduction

Vitamin D is an essential fat-soluble vitamin involved in calcium and bone metabolism. Scientific studies in recent years have shown that its deficiency is associated with chronic disorders such as hypertension, obesity, diabetes mellitus, metabolic syndrome, cancer, coronary artery disease (CAD), autoimmune diseases, infectious diseases, sarcopenia and other musculoskeletal problems.[1–4] Of note, these are important conditions as regards morbidity and mortality. In addition, vitamin D deficiency is very common i.e. estimated to be in approximately one billion people worldwide - also considered as a pandemic.[2,5,6] According to recent studies, there is a high rate of vitamin D deficiency in Turkey, as well. A meta-analysis including 40 studies with a sample size of 111,582 found that the prevalence rate

Abbreviations: COPD, Chronic obstructive pulmonary disease; CAD, Coronary artery disease; 25(OH), 25-hydroxy vitamin D

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of vitamin D deficiency (<20 ng/ml) was 63% for the overall population in Turkey.[7] In a retrospective study from Turkey (with 920 adult women), 90.8% had vitamin D deficiency, and 50.3% had severe vitamin D deficiency.[8]However, a study from Ankara (the capital)including 420 subjects over 65 years of age found that 33.4% of the subjects had vitamin D deficiency(<15 ng/ml).[9]

The majority of studies investigating the relationship between vitamin D and mortality show that mortality is significantly increased in individuals with low 25(OH) vitamin D levels. In a meta-analysis of more than 800,000 participants, there was a significant difference in the relative risk of death between the groups with lowest and highest vitamin D levels, and each decrease in 25(OH) vitamin D levels was associated with increased all-cause mortality.[10]

With the recent COVID-19 pandemic (that started at the end of 2019), 510 million people have been infected with 6.22 million deaths. Hereby, in addition to several abovequoted disorders, the association of vitamin D with COVID-19 has also been questioned/discussed. Vitamin D, which is previously known to reduce the risk of infection by various mechanisms, is thought to be effective in COVID-19 with similar mechanisms. They comprise induction of cathelicidins and defensins which can reduce viral replication rates and decrease concentrations of pro-inflammatory cytokines that produce inflammation.Vitamin D also increases the concentrations of anti-inflammatory cytokines.[11,12] Notably, significant relationship was reported between vitamin D deficiency and the incidence of disease as well as its poor prognosis and mortality.[13,14] However, those studies generally comprised low number of participants from a single center or meta-analysis of studies in different centers.[2,3,13–20] Therefore, reporting (to our best notice) the largest subject population from a single center just beforeand during the pandemic, we tried to explore the association between 25(OH) vitamin D levels and mortality of chronic diseases in subjects aged ≥65 years. This group was taken since they had been in quarantine for a long time and they also had concomitant/chronic diseases. In addition, our examination of the relationship between vitamin D and mortality in this age group (by comparing the pre-pandemic and pandemic periods) will contribute to filling the gap in the relevant literature.

Methods

All adults aged 65 years and above (N = 1949), successively presented to the internal medicine outpatient clinics of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital for any reason between 01 January 2019 to 31 December 2021 were retrospectively analyzed from the hospital electronic database. All subjects with vitamin D measurement (N = 2155) were followed as a cohort from the date of serum vitamin D analysis through death date or 01.01.2022, whichever came the first; for individuals with repeated vitamin D measurements, only the first vitamin D measure was considered for statistical analysis.The results were obtained from a single center. Total 25(OH) vitamin D was measured by CMIA (ChemiLuminescence Microparticle Immunoassay with the Abbott Alinity) biochemistry analyser system which has been standardized in accordance with NIST SRM 2972 (National Institute of Standards & Technology Standard Reference Material 2972) and calibrated at regular intervals. On the other hand, as hemoglobin (Hb) level is also a good surrogate for investigating malnutrition status, we also examined the relationship between anemia (Hb <13 g/dl for men, 12 g/dl for women[21]) and mortality in our patients. The method was SF cube technology with the Mindray BC-6000 analyzer system, which has been standardized/calibrated at regular intervals.

Subjects who had a diagnosis of cancer, hyperparathyroidism, hypoparathyroidism, chronic kidney disease or unexplained hypercalcemia were excluded from the study. Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of our hospital (2021–08/1354).

Age, gender, chronic diseases, survival status, date of death of the deceased, laboratory values including complete blood count, liver/renal functions and 25(OH) vitamin D levels were all noted. According to the relevant literature, subjects were classified into three groups according to their 25(OH) vitamin D levels; severe deficient group (<10 ng/ml), moderate deficient group (10–19.9 ng/ml), and control group (≥20 ng/ml).[10]

Statistical analysis

Statistical analysis was done using SPSS 23.0 package program. Demographics were expressed by mean ± standard deviation for continuous variables and by frequency for qualitative data. Normal distribution was assessed using Kolmogorov–Smirnov test. Between–group comparisons were done by Student's t or Mann-Whitney U tests, as appropriate. Chi–Square, Fisher's exact test or McNemar-Bowker test was used to investigate the relationship between categorical data. When examining the relationship between 25(OH) vitamin D level and death, age, gender, and commonly seen comorbidities (observed at least about 50 times or more) were considered as potential confounders, and were controlled for multivariate analysis. The period before and after 11.03.2020, when the first case of COVID-19 was officially reported in Turkey, was classified as pre-pandemic and pandemic period, and statistical analysis was conducted separately for these periods. The possible factors identified in the univariate analyses were further entered into the Cox regression analyses to determine the independent predictors of death. Anemia status was also added to the Cox regression model to examine the relationship between vitamin D deficiency and death during pre-pandemic and pandemic periods to control the effect of nutritional status. However, the model stability could not be achieved for the pre-pandemic period. Therefore, a common model has been established for all periods (Table 3, Model 2). Statistical significance was set at p <0.05 two-sided.

Results

Data of 1949 subjects were included in this retrospective analysis and 206 of them (10.6%) had at least two vitamin D measurements. Until the time of data collection (01.01.2022), 94 of the cases had died within the aforementioned three years, and only five of them had repeated measurements. The median follow-up period of the patients after the first vitamin D measurement was 361 (8–1118) days. The median time between the second and the first measurements of 163 subjects with 25(OH) vitamin D levels at least twice was 274 (27–947) days. Comparison of the clinical variables between patients who survived and those who died is given in Table 1. While the mean vitamin D level was lower, age and frequency of dyslipidemia, CAD, chronic obstructive pulmonary disease (COPD), arrhythmia, dementia, anemia and severe vitamin D deficiency were higher in subjects who died (all p<0.05).

Among subjects in whom 25(OH) vitamin D measurements were made at least twice, an improvement was observed in the groups with moderate and severe deficiency compared to the first vitamin D measurement. This improvement was seen in both groups who received and did not receive vitamin D supplementation, but this effect was more pronounced in patients who received vitamin D supplementation (Table 2).

When the cumulative hazard function of death was examined according to the vitamin D status (measured at hospital admission), it was found that the severe vitamin D deficient group (10 ng/ml) had a higher probability of death (Log-rank test p = 0.048) (Fig. 1). According to the Cox proportional hazards model (Table 3); age, presence of CAD, COPD, arrhythmia, dementia, anemia and severe vitamin D deficiency were independently/positively related with the mortality (all p<0.05). After adjusted by age, gender and comorbidities, the

Table 1
Comparison of the clinical variables between patient groups.

Characteristic	Died	Survived	p
N	94	1855	
Age, *year**	79.0 (74.0–82.0)	72.0 (67.0–77.0)	<**0.001**
Gender, *male*	25 (26.6)	437 (23.6)	0.499
Hypertension	69 (73.4)	1378 (74.3)	0.849
Diabetes mellitus	38 (40.4)	717 (38.7)	0.731
Dyslipidemia	27 (28.7)	367 (19.8)	**0.035**
CAD	35 (37.2)	397 (21.4)	<**0.001**
Hypothyroidism	13 (13.8)	376 (20.3)	0.128
Bronchial asthma	6 (6.4)	71 (3.8)	0.268**
COPD	15 (16.0)	78 (4.2)	<**0.001****
Arrhythmia	20 (21.3)	84 (4.5)	<**0.001**
Dementia	10 (10.6)	37 (2.0)	<**0.001****
Anemia	39 (47.6)	292 (17.6)	<**0.001**
25 OH vitamin D, *ng/ml**	12.4 (7.7–20.1)	15.2 (9.3–23.9)	**0.010**
No deficiency	23 (24.5)	638 (34.4)	**0.045**
Moderate deficiency	34 (36.2)	687 (37.0)	
Severe deficiency	37 (39.4)	530 (28.6)	

N; number, CAD; coronary artery disease, COPD; chronic obstructive pulmonary disease.
* Median (Q1-Q3).
** Fischer's exact test.

Table 2
The effect of vitamin D supplementation on 25(OH) vitamin D2 levels in patients with at least two measurements.

Vitamin D supplements			
	Second 25(OH) Vitamin D2		
First 25(OH) Vitamin D2	No deficiency	Moderate deficiency	Severe deficiency
No deficiency	21 (61.8)	11 (32.4)	2 (5.9)
Moderate deficiency	25 (67.6)	11 (29.7)	1 (2.7)
Severe deficiency	14 (37.8)	12 (32.4)	11 (29.7)
McNemar-Bowker test *p* <0.001			
No Vitamin D supplements			
	Second 25(OH) Vitamin D2		
First 25(OH) Vitamin D2	No deficiency	Moderate Deficiency	Severe deficiency
No deficiency	15 (78.9)	4 (21.1)	–
Moderate deficiency	7 (43.8)	8 (50.0)	1 (6.3)
Severe deficiency	3 (18.8)	8 (50.0)	5 (31.3)
McNemar-Bowker test *p* = 0.026			

probability of death was found to be 1.91 (95% CI=1.12–3.24) times higher in the severe deficient group (Table 3, Fig. 2). When anemia was also included into the analyses (Table 3, Model 2), the probability of death was found to be 2.19 (95% CI=1.22–3.93) times higher in the moderate deficient group (Table 3, Model 2).

Table 3
Cox Proportional Hazards Model of the association between point prevalence of vitamin D deficiency at admission and exitus.

	Model 1			Model 2		
	HR	CI	p	HR	CI	p
Age, *year*	1.09	1.05 – 1.12	<**0.001**	1.08	1.05 – 1.12	<**0.001**
Male gender	1.24	0.77 – 1.99	0.38	1.15	0.70 – 1.90	0.60
Hypertension	0.74	0.45 – 1.19	0.21	0.67	0.41 – 1.11	0.12
Diabetes mellitus	1.20	0.78 – 1.85	0.41	1.00	0.62 – 1.61	0.99
Dyslipidemia	1.45	0.90 – 2.33	0.13	1.57	0.95 – 2.62	0.081
CAD	1.91	1.23 – 2.98	**0.004**	2.21	1.37 – 3.55	**0.001**
Hypothyroidism	0.76	0.42 – 1.40	0.38	0.73	0.37 – 1.44	0.91
Bronchial asthma	1.99	0.85 – 4.65	0.11	1.32	0.41 – 4.27	0.65
COPD	2.21	1.25 – 3.92	**0.007**	1.88	0.97 – 3.64	0.062
Arrhythmia	4.54	2.72 – 7.58	<**0.001**	3.26	1.82 – 5.83	<**0.001**
Dementia	3.58	1.76 – 7.24	<**0.001**	3.61	1.73 – 7.55	<**0.001**
Anemia	–	–	–	2.73	1.74 – 4.29	<**0.001**
Moderate vitamin D deficiency	1.40	0.82 – 2.39	0.23	2.19	1.22 – 3.93	**0.009**
Severe vitamin D deficiency	1.91	1.12 – 3.24	**0.017**	1.56	0.87 – 2.82	0.14

HR; hazard ratio, CI; 95% confidence interval, CAD; coronary artery disease, COPD; chronic obstructive pulmonary disease.

When subgroup analyzes are made according to pre-pandemic and pandemic periods (Tables 4 and 5 and Figs. 3 and 4), moderate and severe vitamin D deficiency seems to be unrelated to death in the pre-pandemic period (both $p>0.05$), whereas severe (but not moderate ($p = 0.079$)) vitamin D deficiency seems to be more associated with death during the pandemic period ($p = 0.025$).

Discussion

The results of this study have shown that - after having adjusted for potential factors - severe vitamin D deficiency (<10 ng/ml) seems to be an independent predictor for non-cancer mortality. The association between severe vitamin D deficiency and mortality was significant during the pandemic but not before.

Vitamin D deficiency is very common i.e. estimated to be present in approximately one billion people worldwide, also considered as a pandemic.[13,14] Recent scientific studies have shown that it is associated with chronic disorders and mortality.[1–4] A meta-analysis including 73 cohort studies (N = 849,412) found that the relative risk of mortality in the third group with the lowest baseline vitamin D was 1.35 (95% CI=1.22–1.49) times higher than in the top third with high vitamin D levels after adjusted with potential risk factors.[10] The relative risk of mortality increased by 1.50 (95% CI=1.21–1.87) when

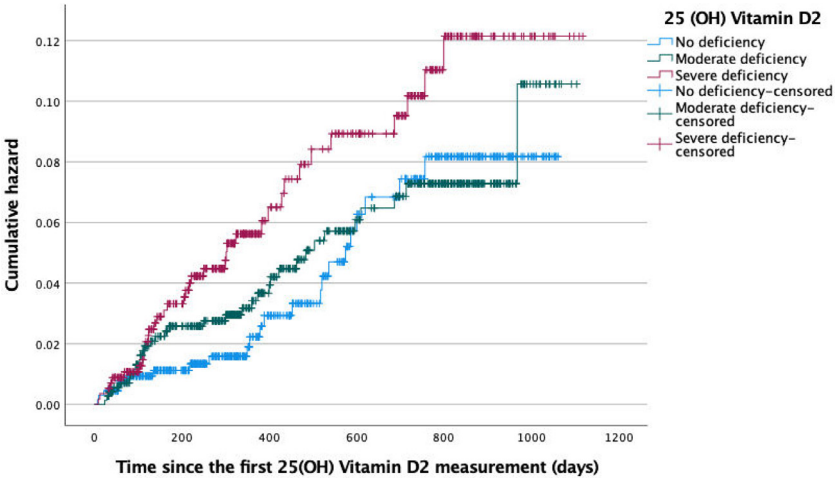

Fig. 1. Cumulative hazard estimates of death in groups with different 25(OH) vitamin D deficiency.

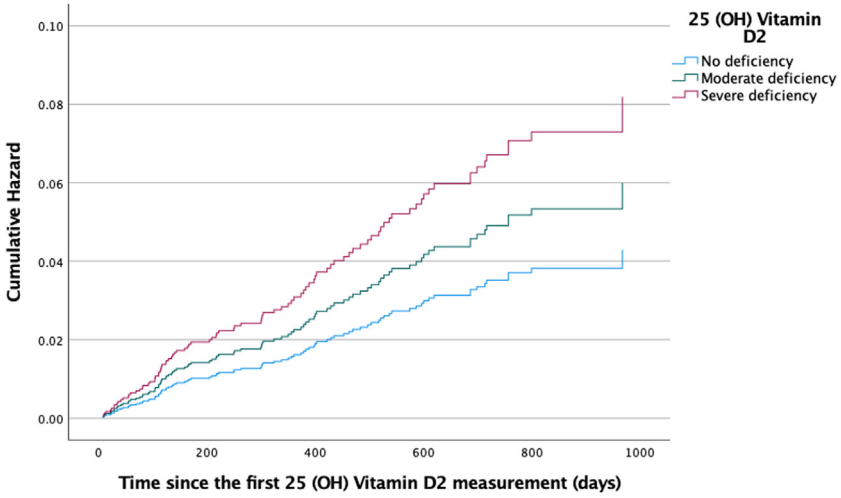

Fig. 2. Cumulative hazard estimates of death in groups with different 25(OH) vitamin D deficiency adjusted by age, gender, hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, hypothyroidism, bronchial asthma, chronic obstructive pulmonary disease, arrhythmia, and dementia.

Table 4
The prevalence of 25(OH) vitamin D2 deficiency at admission in survived vs. died patients during pre-pandemic and pandemic periods.

	25 (OH) Vitamin D2	Died n (%)	Survived n (%)	RR (CI)	p
Pre-pandemic period	Severe deficiency	18 (9.8)	166 (90.2)	1.21 (0.63 – 2.32)	0.56
	Moderate deficiency	19 (7.0)	253 (91.9)	0.86 (0.45 – 1.65)	
	No deficiency	15 (8.1)	170 (91.9)	1.00	
Pandemic period	Severe deficiency	19 (5.0)	364 (95.0)	**2.95 (1.31 – 2.67)**	**0.025**
	Moderate deficiency	15 (3.3)	434 (96.7)	1.99 (0.85 – 4.64)	
	No deficiency	8 (1.7)	468 (98.3)	1.00	
Total	Severe deficiency	37 (6.5)	529 (93.5)	**1.89 (1.14 – 3.14)**	**0.045**
	Moderate deficiency	34 (4.7)	684 (95.3)	1.37 (0.82 – 2.30)	
	No deficiency	23 (3.5)	642 (96.5)	1.00	

RR; Risk ratio, CI; 95% confidence interval.

Table 5
Cox Proportional Hazards model of the association between point prevalence of vitamin D deficiency at admission and exitus during pre-pandemic and pandemic periods.

	Pre-pandemic period			Pandemic period		
	HR	CI	p	HR	CI	p
Age, *year*	1.09	1.04 – 1.13	<**0.001**	1.09	1.05 – 1.14	<**0.001**
Male gender	1.07	0.50 – 2.25	0.87	1.33	0.69 – 2.58	0.40
Hypertension	0.46	0.24 – 0.87	**0.017**	1.26	0.55 – 2.92	0.57
Diabetes mellitus	1.28	0.70 – 2.34	0.43	1.23	0.65 – 2.33	0.53
Dyslipidemia	1.47	0.74 – 2.91	0.27	1.30	0.65 – 2.60	0.45
CAD	1.91	1.02 – 3.59	**0.043**	1.97	1.02 – 3.79	**0.044**
Hypothyroidism	1.04	0.49 – 2.20	0.91	0.50	0.17 – 1.45	0.20
Bronchial asthma	1.44	0.43 – 4.88	0.57	2.16	0.60 – 7.72	0.24
COPD	2.15	1.00 – 4.59	**0.049**	2.62	1.06 – 6.50	**0.038**
Arrhythmia	4.18	2.07 – 8.44	<**0.001**	5.41	2.48 – 11.83	<**0.001**
Dementia	1.90	0.63 – 5.72	0.25	6.31	2.45 – 16.23	<**0.001**
Moderate deficiency	1.07	0.53 – 2.15	0.85	2.20	0.91 – 5.32	0.079
Severe deficiency	1.33	0.65 – 2.71	0.43	2.63	1.13 – 6.12	**0.025**

HR; hazard ratio, CI; 95% confidence interval. [a]CAD; coronary artery disease, COPD; chronic obstructive pulmonary disease.

[a] First of all, thank you for your technical support. We fixed some of the things we observed. We made some changes in the spelling of departments. We fixed some misspellings and references. I am writing some deficiencies that we cannot fix. When we look at it in PDF format, some numbers appear on the bottom line in Table 3,4,5. Tables can be more understandable if the numbers are on the same line.

participants with 25(OH) vitamin *D* <10 ng/ml and those with ≥30 ng/ml were compared. Assuming a linear relationship between vitamin D status and mortality, each decrease in 25(OH) vitamin D levels was associated with increased all-cause mortality.[10] A second meta-analysis including 32 cohort studies (*N* = 500,000), found that the relative risk of mortality between participants with 25(OH) vitamin D lowest (0–9 ng/ml) and participants with >30 ng/ml was 1.9 (95% CI=1.6–2.2).[11] Another meta-analysis including 52 trials (*N* = 75,454) found that vitamin D supplementation was not associated with all-cause mortality, cardiovascular/non-cardiovascular or non-cancer mortality.[17]

With the recent COVID-19 pandemic, the association of vitamin D with the COVID-19 has also been questioned/discussed. A meta-analysis of 26 studies (including 8176 COVID-19 patients) found that vitamin D deficiency was not associated with a higher risk of COVID-19 infection, but that severe cases of COVID-19 had 64% (OR=1.64; 95% CI= 1.30–2.09) more vitamin D deficiency compared with the mild cases.[18] In the same meta-analysis, vitamin D deficiency was found to increase the hospitalization risk (OR=1.81, 95%CI=1.41–2.21) and mortality from COVID-19 (OR=1.82, 95%CI=1.06–2.58).[18] In another study, it was observed that there was a negative correlation between levels of mean vitamin D and number of cases of COVID-19/1 M population in each country, and between the mean vitamin D levels and the number of deaths caused by COVID-19/1 M.[19] On the other hand, a recent study found that vitamin D deficiency was not associated with COVID-19 infection, but severe vitamin D deficiency may increase risk for mortality.[20] A recent study from Turkey reported that the mean serum 25(OH) vitamin D level was found to be lower in severe-critical COVID-19 patients compared to moderate-level COVID-19.[22] In another study, it was observed that vitamin D treatment shortened the hospital stay and reduced mortality in COVID-19, even in the presence of comorbidities.[23] The relationship between vitamin D deficiency and COVID-19 disease, and the prevalence of COVID-19 show conflicting findings in many studies. Notably, regional and temporal differences in the number of COVID-19 cases during the pandemic might have played role in this regard. Herewith,

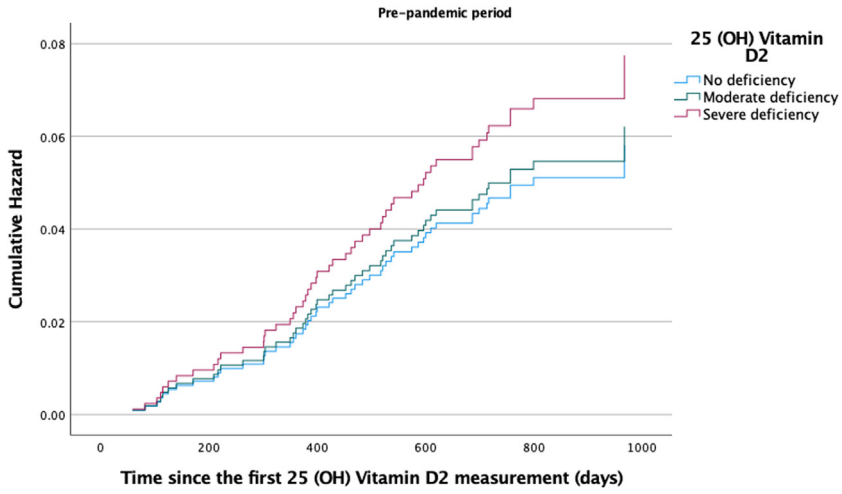

Fig. 3. Cumulative hazard estimates of death in groups with different 25(OH) vitamin D deficiency adjusted by age, gender and all comorbidities during the pre-pandemic period.

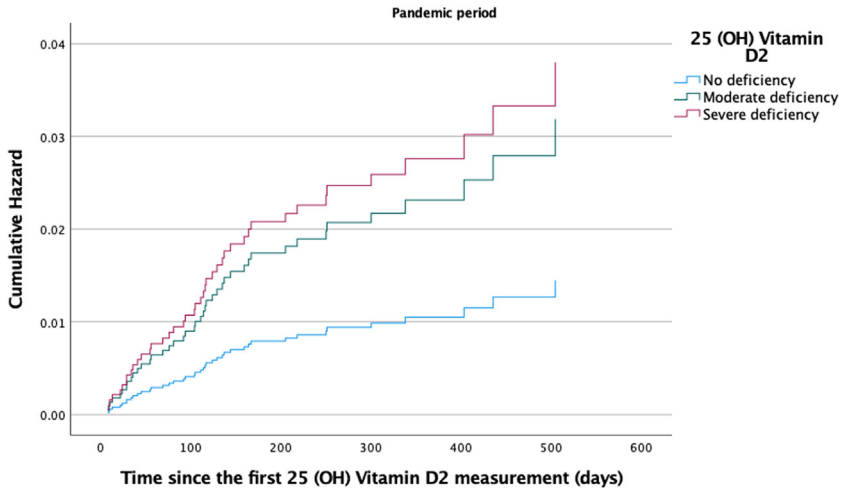

Fig. 4. Cumulative hazard estimates of death in groups with different 25(OH) vitamin D deficiency adjusted by age, gender and all comorbidities during the pandemic period.

significant relationship between vitamin D deficiency and the disease prognosis/mortality was similarly observed among them.[18–20,22,23] Additionally, in another study from southeast Turkey, vitamin D deficiency was found to be indifferent between the pre-pandemic and pandemic periods (Apr 2017 - May 2020) in adult females.[8] In our study (from central Turkey), it was observed that there was a decrease in the rate of vitamin D deficiency during the pandemic period (Mar 2020 - Jan 2022) compared to the pre-pandemic period (Jan 2019 - Mar 2020) in older adults. This finding might have been related to the fact that physicians and the society are more sensitive to vitamin D deficiency (especially in the elderly) during the pandemic. For sure; differences in age, gender, culture, socioeconomic status, educational level and clothing style of the study population and regional/temporal differences could have again been contributory.

The results of our study have shown that - independent of all diseases - the relative risk of all-cause mortality between participants with severe vitamin D deficiency (25(OH) vitamin D <10 ng/ml) and those with ≥20 ng/ml was 1.91 (95%CI=1.12–3.29). In addition; age, presence of CAD, arrhythmia, COPD, anemia or dementia were found to be significantly associated with mortality. However, moderate vitamin D deficiency (10–19.9 ng/ml) was not associated with mortality.

Among subjects in whom 25(OH) vitamin D measurements were made at least twice, an improvement was observed in groups with moderate and severe deficiency - compared to the initial vitamin D measurement. While both groups i.e. who received vitamin D supplementation and those who did not showed similar response, the improvement was more pronounced in the former group. In our opinion, awareness concerning vitamin D could have been the possible reason for this finding. Yet, even in the absence of supplementation, those subjects could have applied for routine controls/measurements to assess their vitamin D status (under routine sunbathing and appropriate nutrition intake).

An important finding of this current study is that - after the first 25(OH) vitamin D measurement - subjects with severe deficiency had significantly higher probability of death when the cumulative hazard function of death was analyzed according to the vitamin D deficiency status during the follow-up (Fig. 1). However, when subgroup analysis was performed, the association between severe vitamin D deficiency and mortality was not significant before the pandemic - but was significant during the pandemic. This might be related to transportation problems during the pandemic, the inability of patients to receive adequate treatment, the deterioration of chronic diseases such as hypertension, diabetes mellitus (due to long immobilization periods), and the presence of severe COVID-19 diseases (Figs. 3 and 4). However, in multivariate Cox regression with adjustment for such potential confounders, the association remained statistically significant. Therefore, the high negative association between vitamin D and mortality could have been attributed to

increased COVID-19 fatality among individuals with vitamin D deficiency. In this study, we could not differentiate the proportion of COVID-19 related death numbers, though. This finding seems to be inconsistent with meta-analyses that found a significant relationship between vitamin D deficiency and mortality in the pre-pandemic period.[10,17] It might have been related to the fact that our study population was composed of elderly who - as mentioned above - had increased frailty during the pandemic. In fact, one of the important contributions of this study to the literature is that we questioned how elderly (the most vulnerable population) was affected by the COVID-19 pandemic. With its data on the relationship between vitamin D deficiency and mortality before and during the COVID-19 pandemic, our results could add further to the previous/pertinent literature.

In our study, we did not examine the relationship among nutritional status of patients, infections and mortality, which might be important for mortality. Missing covariates such as taking vitamin D supplement, COVID-19 or other infection were another limitation. Additionally,to be cross-sectional and retrospective design would be the other limitations of our study. Moreover, except a few reports,[24,25] there is a big gap in the literature for prospective studies on vitamin D, COVID-19 and mortality. For sure, future longitudinal analyses encompassing larger group of participants will make significant contributions to practice and research alike.

In conclusion, vitamin D measurement/treatment is very easy and cheap where, on the contrary, severe vitamin D deficiency can be quite mortal. The importance of vitamin D as regards mortality and the course of chronic diseases was shown in this study once again. Accordingly, vitamin D is an important parameter that should be included in every clinician's holistic approach in daily clinical practice.

Authors' contribution

Substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data: MED, OK, MK, TCK, FES, MD, AS, BC, LO. Drafting the article or revising it critically for important intellectual content: MED, OK, MK, TCK, FES, MD, AS, BC, LO. Final approval of the version to be published: MED, OK, MK, TCK, FES, MD, AS, BC, LO.

Ethics declarations

Ethical statement

The study complied with the existing ethical standards. Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of our hospital (2021−08/1354).

Human and animal rights

Considering the design of the study no human or animal rights were infringed upon.

Informed consent

Considering the design of the study no informed consent was necessary.

Declaration of Competing Interest

There are no conflicts of interest.

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None.

Sponsor's role

None.

Funding sources

None.

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