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# Is vitamin D level important in pregnant women with COVID-19?

Ahmet Değirmenci[1], Sertaç Ayçiçek[2], Fatih Mehmet Fındık[3], Mulaim Sizer[4]
Azize Pervin Değirmenci[5], Pelin Değirmenci Ayçiçek[2], Çiğdem Mermutluoğlu[5]

[1]Department of Obstetrics and Gynecology, Ergani State Hospital, Diyarbakır, Turkiye
[2]Department of Obstetrics and Gynecology, Diyarbakır Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkiye
[3]Department of Obstetrics and Gynecology, Faculty of Medicine, Dicle University, Diyarbakır, Turkiye
[4]Department of Obstetrics and Gynecology, Batman Training and Research Hospital, Batman, Turkiye
[5]Department of Infectious Disease and Clinical Microbiology, Faculty of Medicine, Dicle University, Diyarbakır, Turkiye

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**Corresponding Author**: Mulaim Sizer , mulayimsizer@hotmail.com

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## ABSTRACT

**Aim:** The COVID-19 pandemic started in Wuhan City, Hubei Province, China in late December 2019. In our study, we aimed to evaluate the effectiveness of vitamin D levels on the clinic of the disease, laboratory findings, severity of the disease and, length of hospital stay by grouping pregnant patients with a diagnosis of COVID-19 according to their vitamin D levels.

**Methods:** A total of 125 patients were included. According to the vitamin D levels of the patients at the time of hospitalization, two groups were determined as below and above 20ng/ml, which is the limit of vitamin D deficiency. The patients in these two groups were compared in terms of demographic features, clinical findings, laboratory findings, imaging findings, hospitalization times and need for intensive care.

**Results:** When evaluated according to serum 25 hydroxyvitamin D level, patients' fever, pulse, oxygen saturation, the severity of lung involvement in computed tomography, hospitalization there was no statistically significant difference between the groups in terms of duration and need for intensive care. When the laboratory parameters of the patients at hospitalization were compared according to serum 25 hydroxyvitamin D levels, there was no statistically significant difference between the two groups in terms of any laboratory parameter. As a result of the analysis, only lymphocyte count was determined as the independent variable affecting the severity of lung involvement in thorax CT (Computed tomography). As the lymphocyte count decreased, the severity of involvement in thorax CT increased.

**Conclusion:** Our study showed that vitamin D level did not have a significant relationship with any of the parameters related to COVID-19 such as clinical and laboratory findings, severity of the disease and duration of hospitalisation. It is also supported by our study that the decrease in lymphocyte counts is associated with severe COVID-19 disease.

**Keywords:** Vitamin D, pregnancy, COVID-19

## INTRODUCTION

Cases of pneumonia of unknown etiology were reported in Wuhan city, Hubei Province, China in December 2019 and it was observed that the disease spread rapidly. Fever, shortness of breath and cough were the common features of the cases. It was determined that those who died from the disease were mostly elderly patients with comorbidities. As a result of the studies carried out to identify the agent, it was observed that the disease agent was a new type of coronavirus similar to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), and its name was determined as 'Severe Acute Respiratory Syndrome coronavirus 2' (SARS-CoV-2), and the disease was called 'COVID-19' as an abbreviation of the words 'Coronavirus disease 2019.[1] The disease spread all over the world in a short time and was declared a pandemic by the World Health organization (WHO) on 11 March 2020.[2]

According to WHO data, more than 263 million cases and more than 5 million deaths were reported until December 2021, and it is estimated that the actual number of cases and deaths is much higher than reported.

SARS-COV-2 is a single-stranded, enveloped RNA virus. It is a zoonotic virus and is transmitted by droplet. It binds to the cells it will infect with angiotensin converting enzyme-2 (ACE-2) receptor.[3] The most common symptoms of the disease are fever, cough and malaise. The most common laboratory findings are lymphopenia, elevated C-reactive protein (CRP) and elevated erythrocyte sedimentation rate. The clinical presentation of patients varies as asymptomatic, mild disease, severe disease and critical disease. The severity of the disease is associated with advanced age, comorbidities

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(diabetes, hypertension, obesity, chronic kidney disease, chronic respiratory diseases, malignancies) and male gender.[4,5] So far, there is no antiviral treatment with proven efficacy. Physiological changes that occur during pregnancy make pregnant women more vulnerable to viral infections. Although it was thought that pregnant women survived the COVID-19 disease more mildly at the beginning of the pandemic, as a result of extensive studies conducted in the following periods, it was stated that the disease had a more severe course in pregnant women compared to non-pregnant women and caused more deaths.[6,7]

Immunomodulatory activity of vitamin D is known. It decreases proinflammatory cytokines (T helper 1, Interleukin-2, TNF alpha and Interferon gamma) and increases antiinflammatory cytokines (Interleukin 4, Interleukin 5 and Interleukin 10). This has been thought to be preventive and therapeutic against the hyperinflammation state called 'cytokine storm', a complication of COVID-19 disease. Vitamin D also increases the production of antimicrobial peptides such as cathelicidin and defensin. Especially cathelicidin shows antiviral activity by acting on the envelopes of viruses. This feature has shown that vitamin D is protective against respiratory tract viruses.[8-12]

In our study, we aimed to evaluate the effects of vitamin D levels of pregnant patients diagnosed with COVID-19, who were grouped according to vitamin D levels, on the clinic, laboratory findings, severity of the disease and duration of hospitalisation.

## METHODS

The study was carried out with the permission of the Gazi Yaşargil Training and Research Hospital Non-Interventional Clinical Researches Ethics Committee (Date: 27/07/2021 Decision No: E-58146266) and Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 27/05/2021 Decision No: 339). All procedures were carried out in accordance with the ethical rules and principles of the Declaration of Helsinki.

Our study was conducted between March 2020 and January 2021 on pregnant patients hospitalised due to COVID-19 disease in Dicle University Faculty of Medicine Pandemic Hospital and Diyarbakır Health Sciences University Gazi Yaşargil Training and Research Hospital Gynecology and Obstetrics Clinic (ward or intensive care unit).

Our study was a retrospective study and patient data were obtained from patient files obtained from the archives of the hospitals. A total of 125 patients from Dicle University Faculty of Medicine and Diyarbakır Health Sciences University Gazi Yaşargil Training and Research Hospital were included in our study.In our study, according to the vitamin D levels of pregnant patients hospitalised due to COVID-19 in both hospitals at the time of hospitalisation, two groups were determined as below and above the vitamin D deficiency limit of 20ng/ml. Age (years), trimester of pregnancy, gravidity and parity, body mass index (BMI) (kg/m$^2$), vital signs; fever, pulse rate, arterial blood pressure (mm/hg), oxygen saturation, severity of involvement on thorax CT (mild, moderate, severe), whether they needed intensive care, which treatment was given, duration of hospitalisation (days), laboratory values during hospitalisation and discharge; CRP, D-dimer, INR, ferritin, troponin I, procalcitonin, MPV, PLT, WBC, lymphocyte, monocyte, eosinophil, haemoglobin and platelecrit were compared.

### Inclusion Criteria For Our Study;

- Having a live, intrauterine pregnancy confirmed definitively by ultrasonography.
- Having a positive COVID-19 RT-PCR test result or a negative test result but diagnosed as COVID-19 with thorax CT, clinical and laboratory findings.
- Patients do not have other chronic diseases that may affect their clinical course and vitamin D levels (hypertensive diseases, diabetes mellitus, heart diseases).

Vitamin D levels of our patients were determined by measuring 25 hydroxyvitamin D level in blood. A 2cc blood sample was collected in a biochemistry tube. Vitamin D was measured with Shimadzu's HPLC 20AT device. Results were given as ng/ml. All laboratory variables except serum 25 hydroxyvitamin D were measured both at admission and discharge, 25 hydroxyvitamin D was measured only at hospitalization. Laboratory values at hospitalization and discharge were compared. Pregnancy and gestational age of our patients were determined by last menstrual period (LMP), previous ultrasonography (USG) data and fetal USG measurements with GE Voluson E8 Ultrasound device (year of manufacture 2015). The lung involvement of COVID-19 in the thorax CT scans of our patients was divided into 3 categories as mild, moderate, and severe involvement as determined by radiology units. The clinical course of our patients was evaluated according to the follow-up of vital signs, duration of hospitalization and the need for intensive care. The classification of the disease as mild or severe was not done due to the fact that the physicians working in our clinics were constantly changing due to the pandemic working order and that a standardization could not be achieved due to the two different hospitals.

COVID-19 diagnoses of our patients were determined according to the COVID-19 RT-PCR test results of Dicle University Faculty of Medicine Microbiology Laboratory and Diyarbakır Provincial Health Directorate Public Health Laboratory. 115 patients with positive test results and 10 patients with negative test results but whose thorax CT, clinical symptoms and laboratory findings were compatible with COVID-19 disease were included in the study.

### Statistical Analysis

The conformity of continuous variables to normal distribution was analysed by Shapiro-Wilk test. Continuous variables were expressed using mean ± standard deviation or median (minimum-maximum) values. According to the results of the normality test, mann whitney U test and Independent Paired sample t test were used for comparisons between groups. Categorical variables were analysed using chi-square test, fisher's exact chi-square and fisher-freeman-halton tests. The difference score value was calculated in order to examine the change in the final measurements compared to the initial measurements, and intergroup comparisons of these

measurements were made using the mann-whitney U test and the independent paired sample t test. Wilcoxon signed ranks test and dependent sample t test were used to compare laboratory values at hospitalisation and discharge. Linear regression analysis was performed to investigate the factors that may be effective on length of hospitalisation. As a result of the univariate linear analysis, those with a p value less than 0.250 were included in the multiple linear analysis test. Among the correlated values, those with clinical significance were included in the analysis. An ordinal regression analysis was performed to investigate the factors that may be effective on the severity of lung involvement in thorax computed tomography. Among the highly correlated values, only those with clinical significance were included in the analysis.For statistical analyses, SPSS (IBM corp. released 2012. IBM SPSS statistics for windows, version 21.0. armonk, NY: IBM Corp.) programme was used and type I error level was accepted as 5% in statistical analyses.

## RESULTS

Of the 125 pregnant patients included in the study, the median age was 29 years. 15-43 C ovid-19 virus PCR test positivity was detected in 115 (92%) of a total of 125 patients. The results of computerised thorax tomography were graded as mild, moderate and severe according to the severity of the findings. Demographic data and clinical features of the patients are shown in Table 1.

Patients were divided into two groups as lower than 20 ng/ml and higher than 20 ng/ml according to serum 25 hydroxyvitamin D level. There was no statistically significant difference between these groups in terms of age, BMI, trimester of pregnancy, number of gravities and parities, fever, pulse rate, oxygen saturation, COVID-19 virus PCR test positivity, severity of lung involvement on computerised thoracic tomography (Figure 1), lenght of hospitalisation (Figure 2) and need for intensive care (Table 2).

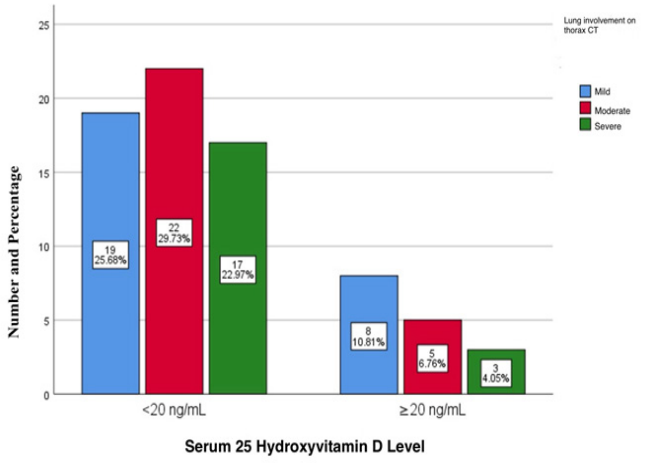



**Figure 1.** Severity of lung involvement on thorax CT according to serum 25 hydroxyvitamin D level grouping

When the laboratory parameters of the patients at the time of hospitalisation were compared according to serum 25 hydroxyvitamin D level grouping, there was no statistically significant difference between the two groups in terms of any laboratory parameter.

Table 1. Age, BMI averages, trimester of pregnancy, parity and clinical characteristics of the patients

| Parameter | Values (n=125) |
|---|---|
| Age (years) | 29.3±6.0 |
| BMI (kg/m2) | 22.1 (18.3-34) |
| **Pregnancy trimester (n=124)** | |
| I | 18 (%14.4) |
| II | 17 (%13.6) |
| III | 89 (%71.2) |
| **Gravidity (n=116)** | |
| 1 | 11 (%8.8) |
| 2 | 19 (%15.2) |
| ≥3 | 86 (%68.8) |
| Median value | 3 (1-8) |
| **Parity (n=116)** | |
| 0 | 16 (%12.8) |
| 1 | 29 (%23.2) |
| 2 | 36 (%28.8) |
| ≥3 | 35 (%28) |
| Median value | 2 (0-7) |
| Fever (°C) (n=123) | 36.5 (36-39) |
| Pulse rate (/dk) (n=120) | 88 (70-135) |
| Oxygen saturation (%) (n=123) | 98 (78-100) |
| PCR positivity | 115 (%92) |
| **Severity of lung involvement on thorax CT (n=74)** | |
| Mild | 27 (%21.6) |
| Moderate | 27 (%21.6) |
| Severe | 20 (%16) |
| Lenght of hospitalisation (days) (n=123) | 5 (0-35) |
| Intensive care needs | 18 (%14.4) |

Non-normally distributed data are expressed as median (minimum-maximum). normally distributed data are expressed as mean±st deviation and n (%). BMI: Body mass index

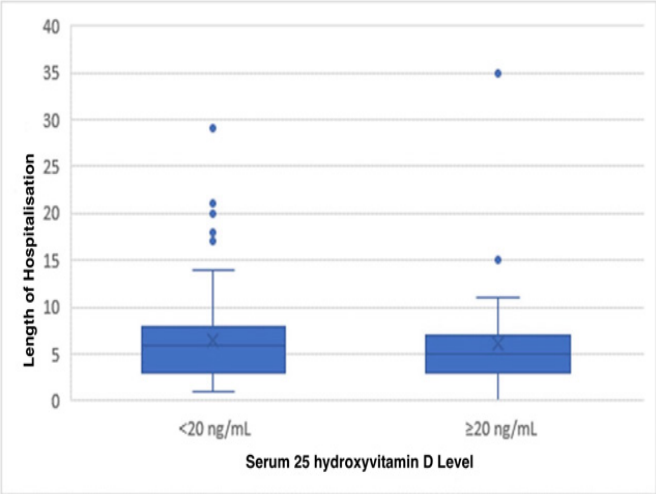



**Figure 2**. Lenght of hospitalisation according to serum 25 hydroxyvitamin D level grouping

Although CRP and D-dimer levels were lower in pregnant women with serum 25 hydroxyvitamin D levels ≥20ng/ml compared to those with levels below 20 ng/ml, this difference was not statistically significant.When we compared the laboratory values of the patients at hospital discharge according to serum 25 hydroxyvitamin D level grouping, there was no statistically significant difference between the two groups in terms of any laboratory value. Pregnant women with low serum 25 hydroxyvitamin D levels had

higher discharge CRP levels than the others. However, this difference was not statistically significant. In addition, no statistically significant difference was found between the serum 25 hydroxyvitamin D level groups in the change in hospitalisation and discharge laboratory values (Table 3).

Tablo 2. Comparison of age, mean BMI, trimester of pregnancy, parity and clinical findings of the patients according to serum 25 hydroxyvitamin D level grouping

| | Serum 25 Hydroxyvitamin D level | | p |
|---|---|---|---|
| | <20 ng/ml (n=89) | ≥20 ng/ml (n=36) | |
| Age (years) | 28 (15-43) | 30 (18-40) | 0.776m |
| BMI (kg/m2) | 22.3 (18.3-34) | 22.1 (19-29) | 0.476m |
| **Pregnancy trimester (n=124)** | | | |
| I | 11 (%12.5) | 7 (%19.4) | |
| II | 13 (%14.8) | 4 (%11.1) | 0.566X² |
| III | 64 (%72.7) | 25 (%69.4) | |
| **Gravidity (n=116)** | | | |
| 1 | 5 (%6) | 6 (%18.2) | |
| 2 | 15(%18.1) | 4 (%12.1) | 0.116X² |
| ≥3 | 63 (%75.9) | 23 (%69.7) | |
| Median value | 3 (1-8) | 3 (1-7) | |
| **Parity (n=116)** | | | |
| 0 | 8 (%9.6) | 8 (%24.2) | |
| 1 | 23 (%27.7) | 6 (%18.2) | |
| 2 | 29 (%34.9) | 7 (%21.2) | 0.089X² |
| ≥3 | 23 (%27.7) | 12 (%36.4) | |
| Median value | 2 (0-7) | 2 (0-5) | |
| Fever (°C) (n=123) | 36.5 (36-39) | 36.5 (36-39) | 0.360m |
| Pulse rate (/dk) (n=120) | 88 (70-135) | 87 (75-125) | 0.146m |
| Oxygen saturation (%) (n=123) | 97 (78-100) | 98 (91-100) | 0.486m |
| PCR positivity | 81 (%91) | 34 (%94.4) | 0.723f |
| | | | |
| **Severity of lung involvement on thorax CT (n=74)** | | | |
| Mild | 19 (%32.8) | 8 (%50) | 0.429X² |
| Moderate | 22 (%37.9) | 5 (%31.3) | |
| Severe | 17 (%29.3) | 3 (%18.8) | |
| Lenght of hospitalisation (days) (n=123) | 6 (1-29) | 5 (0-35) | 0.478m |
| Intensive care needs | 15 (%16.9) | 3 (%8.3) | 0.219X² |

Non-normally distributed data are expressed as median (minimum-maximum), normally distributed data as mean±SD and n (%). m Mann-Whitney U test, X² Chi-square test, f Fisher-Freeman-Halton test. CT: Computed tomography

Enoxaparin Sodium was given to 71.2% (n=89), lopinavir/ritonavir combination to 56% (n=70), hydroxychloroquine sulphate to 8% (n=10), oseltamivir to 4% (n=5). When the treatments administered to the patients were compared according to serum 25 hydroxyvitamin D levels, no statistically significant difference was found between the groups in any of the treatments. Enoxaparin sodium was the most frequently given treatment in both groups. EAS a result of the analysis performed for the factors affecting the lenght of hospitalisation, oxygen saturation and severity of lung involvement on thorax CT were determined as independent variables affecting the duration of hospitalisation (Table 4).

As the severity of lung involvement on thorax CT increased and oxygen saturation decreased, the duration of hospitalisation increased. (Y (length of hospitalisation)= 39.427-(0.460x saturation)+(1.071x severity of AC uptake on thorax CT)

Table 3. Comparison of the changes in the laboratory values of the patients at hospitalisation and discharge between serum 25 hydroxyvitamin D level groups.

| | Serum 25 hydroxyvitamin D level | | p |
|---|---|---|---|
| <20 ng/mL (n=89) | | ≥20 ng/mL (n=36) | |
| Hemoglobin (g/dL) (n=118) | -0.5 (-4.30:2.1) | -0.4 (-3.30:1.4) | 0.730m |
| White blood cell count (10^9/L) (n=118) | 0.99 (-10.34:23.97) | 0.46 (-7.54:15.49) | 0.790m |
| Lymphocyte count (10^9/L) (n=118) | 0.3 (-0.69:2.39) | 0.33 (-0.64:1.75) | 0.728m |
| Monocyte count (10^9/L) (n=119) | 0.11 (-0.42:0.64) | 0.1 (-0.22:10.67) | 0.905m |
| Eosinophil count (10^9/L) (n=119) | 0.01 (-0.16:0.4) | 0.03 (-0.07:0.28) | 0.614m |
| Platelet count (10^9/L) (n=118) | 40 (-133:464) | 25 (-43:180) | 0.808m |
| Mean platelet volume (fL) (n=117) | -0.2 (-2.60:1.4) | -0.1 (-1.30:1.4) | 0.222m |
| PCT (%) (n=99) | -1.7 (-14:9.3) | -2.80 (-8.90:7) | 0.784m |
| C-reaktive protein (mg/dl) (n=116) | -4.75 (-175.70:102.2) | -5.7 (-107:16.7) | 0.436m |
| D-dimer (ng/mL) (n=93) | -97 (-1916:10503) | -84 (-2621:3892) | 0.798m |
| Ferritin (uq/L) (n=99) | 1 (-228:1934) | -2 (-202:117) | 0.408m |
| Troponin I (ng/ml) (n=31) | 0 (-0.07:0.05) | 0 (-0.04:0.01) | 0.884m |
| Procalsitonin (ng/ml) (n=114) | -0.01 (-2.12:8.04) | -0.02 (-0.57:12.88) | 0.803m |
| INR (n=114) | 0 (-0.55:0.65) | 0 (-0.12:0.35) | 0.594m |
| Eosinophil/Monocyte ratio (n=119) | 0.04 (-0.24:1.71) | 0.04 (-0.09:0.56) | 0.394m |

Non-normally distributed data are expressed as median (minimum-maximum). normally distributed data as mean ± standard deviation and n (%). m Mann-Whitney U test, † Independent Paired Sample t Test., PCT: Plateletcrit

Table 4. Variables affecting length of hospitalisation

| Variables | Univariate linear regression | | | Multiple linear regression | | |
|---|---|---|---|---|---|---|
| | B | Std. Error | p | B | Std. Error | p |
| Age | -0.003 | 0.077 | 0.967 | | | |
| BMI | 0.309 | 0.197 | 0.120 | 0.141 | 0.213 | 0.512 |
| Severity of Lung involvement on thorax CT | 2.174 | 0.549 | <0.001 | 1.071 | 0.501 | 0.034 |
| Fever | 2.110 | 0.571 | <0.001 | 0.162 | 0.495 | 0.744 |
| Saturation | -0.472 | 0.135 | 0.002 | -0.460 | 0.125 | <0.001 |
| 25 Hydroxyvitamin D | -0.048 | 0.048 | 0.314 | | | |
| Lopinavir/ritonavir use | 3.168 | 0.879 | <0.001 | 0.860 | 1.078 | 0.429 |
| Hydroxychloroquine sulphate | -0.558 | 1.758 | 0.751 | | | |
| Oseltamivir use | 1.453 | 2.316 | 0.532 | | | |
| Enoxaparin sodium | 2.485 | 0.990 | 0.013 | 2.209 | 1.393 | 0.118 |
| C-reactive protein | 0.027 | 0.012 | 0.024 | 0.012 | 0.010 | 0.239 |
| D-dimer | 0 | 0 | 0.492 | | | |
| Troponin I | -11.529 | 10.988 | 0.296 | | | |
| Mpv | -0.316 | 0.364 | 0.387 | | | |
| Platelet count | -0.004 | 0.006 | 0.568 | | | |
| Lymphocyte count | -2.238 | 0.906 | 0.015 | -0.960 | 0.800 | 0.235 |
| INR | 1.385 | 3.386 | 0.683 | | | |
| PCT | 0.017 | 0.042 | 0.690 | | | |
| Eosinophil/Monocyte ratio | -3.692 | 3.553 | 0.301 | | | |

Adjusted R Square= 0.339, Constant= 39.427. Laboratory values at the time of hospitalisation were taken as laboratory values. CT: Computerised tomography, BMI: Body mass index. Mpv: Mean platelet volume, PCT: Plateletcrit. B: Regression coefficient, Std: Standard

As a result of the analysis performed to determine the variables affecting the severity of lung involvement on thorax CT, only lymphocyte count was determined as the independent variable affecting the severity of lung involvement on thorax CT (Table 5). As the lymphocyte

count decreased, the severity of lung involvement on thorax CT increased.

Table 5. Variables affecting the severity of lung involvement on thorax CT.

| | | Prediction | Wald | 95% CI | p |
|---|---|---|---|---|---|
| Threshold values | Lung involvement severity=1 | -5.325 | 0.462 | -20.675 - 10.025 | 0.497 |
| | Lung involvement severity=2 | -3.424 | 0.192 | -18.736 - 11.889 | 0.661 |
| Variables | Age | -0.014 | 0.105 | -0.095 - .068 | 0.745 |
| | Trimester of pregnancy | 0.161 | 0.237 | -0.488 - 0 .811 | 0.626 |
| | 25 Hydroxyvitami D | -0.020 | 0.482 | -0.075 - 0.036 | 0.487 |
| | C-reactive protein | 0.004 | 0.390 | -.009 - 0.016 | 0.532 |
| | D-dimer | 0.000 | 1.044 | .000 - 0.001 | 0.307 |
| | Saturation | -0.027 | 0.114 | -0.187 - | 0.132 |
| | Eosinophil/ Monocyte ratio | -6.142 | 3.441 | -12.631 - 0.348 | 0.064 |
| | Lymphocyte count | -1.399 | 4.898 | -2.638 - | -0.160 |

Model fit test (pearson) p= 0.559, Parallel curves assumption test p=0.939. Laboratory values were taken as laboratory values at the time of hospitalisation., CI: Confidence interval

## DISCUSSION

Although most of the studies in the literature examining the relationship between vitamin D and COVID-19 argue that vitamin D has a positive effect on infection, disease severity and mortality, there are also studies claiming the opposite. In the meta-analysis conducted by Chen et al,[13] studies involving a total of 536,135 patients until 5 June 2021 were analysed. It was stated that the average age of the patients in the studies was between 49 and 69 years, most studies were conducted in America, 5 studies in Europe, 1 study in Asia and 1 study in Australia. Vitamin D deficiency was accepted as <20ng/ml and insufficiency as 20-30ng/ml, and it was determined that low vitamin D level did not increase the risk of COVID-19 infection and mortality. It was found that each 10ng/ml increase in serum vitamin D level had no effect on infection and mortality, and vitamin D supplementation did not reduce the need for intensive care and mortality. In the study conducted by Hastie et al.[14] the data of 343.484 patients uploaded to the United Kingdom Biobank database were analysed and the relationship between vitamin D level and COVID-19 disease was investigated. It was found that the severity and mortality of COVID-19 disease were associated with advanced age, male gender, black race, obesity and diabetes mellitus, but not with vitamin D level.

Studies have shown that patients with severe COVID-19 disease have lower blood lymphocyte counts compared to other patients.[15] It is thought that the progressive decrease in lymphocyte count may be an early clinical indicator of severe COVID-19 disease.

In the meta-analysis conducted by Meng et al.[16] by analysing 24 studies including 3547 patients, comorbidities, major symptoms, laboratory findings that may be associated with the severity of the disease in patients diagnosed with COVID-19 were tried to be determined. In the study, the rate of severe disease was found to be 30%. 54% of the cases consisted of male gender. As a result of meta-analysis of 24 studies, the most common clinical symptoms were found to be fever 80% and cough 59%. The most common comorbidity was hypertension 19%, diabetes 9%, cardiovascular disease 8%. Patients with chronic respiratory diseases, chronic kidney disease and cardiovascular diseases were found to have a higher risk of progression to severe disease. The common laboratory findings of the patients included in the study were leucopenia, lymphopenia and elevated CRP. Two groups were defined as severe and non-severe disease. The most significant difference between the groups was measured as CRP and CRP values in the severe disease group were found to be 1.66 higher on average than in the non-severe group. Neutrophil/ Lymphocyte ratio and Erythrocyte Sedimentation Rate were also found to be higher in the severe disease group. In a review of 30 studies including 5570 patients, Wang et al.[17] found that the Neutrophil/Lymphocyte ratio was higher in patients with severe disease and its sensitivity and specificity were 82% and 77%, respectively. In our study, similar to the results of this review, we found that the number of lymphocytes decreased as the severity of COVID-19 involvement increased in pregnant women undergoing thoracic CT and the result was statistically significant (p=0.027).

In the study conducted by Sinaci et al.[18] in our country, vitamin D levels of patients hospitalised and planned for treatment due to COVID-19 were found to be statistically significantly lower. In the same study, a statistically significant relationship was examined between the severity of COVID-19 disease and vitamin D level, and accordingly, vitamin D level was found to be significantly higher in patients in the moderate and severe COVID-19 group compared to patients in the mild COVID-19 group. In contrast to the data in this study, no statistically significant finding was found when data that may indicate the course of the disease such as the need for intensive care, COVID-19 involvement in thoracic CT scans, laboratory values, and hospitalisation times of the patients were compared between the two groups with vitamin D levels below and above 20 ng/ml in our study. Although the need for intensive care was 16.9% in the group with vitamin D below 20 ng/ml and 8.3% in the group with vitamin D above 20 ng/ml, this data was not statistically significant.

In the meta-analysis conducted by Oscanoa et al.[19] the relationship of vitamin D with the severity of COVID-19 disease and mortality was investigated. The mean age of the patients was 60.8 years and 53.8% were male. In 17 studies, it was found that 25 hydroxyvitamin D levels below 20 ng/ml were associated with an increased risk of severe COVID-19 disease, and in 13 studies it was associated with increased mortality. 7 studies included CRP values and all of them had values >10mg/L. 7 studies showed that male gender had a higher risk of disease severity and mortality compared to females. Similarly, in 3 studies included in the meta-analysis conducted by Pereira et al.[21] it was found that 25 Hydroxyvitamin D level below 20 mg/ml increased the risk of hospitalization and mortality increased in 5 studies. In the meta-analysis conducted by Kazemi et al.[20] it was found that there was no relationship between vitamin D level and the need for intensive care. In a meta-analysis of more than 10 thousand cases aiming to determine the causes of severe disease in COVID-19 infection, including 61 studies by Fang et al.[22] it was found that advanced age, male gender and the presence of comorbidities (hypertension, diabetes, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, hepatitis B disease) were each

directly related to the severity and prognosis of COVID-19 disease. It was found that chronic kidney disease was the comorbidity that increased mortality the most, and chronic obstructive pulmonary disease was the comorbidity that led to the need for intensive care and mechanical ventilation the most.

In this study, no significant difference was found between the groups with vitamin D levels above 20 ng/ml and below 20 ng/ml in terms of the need for intensive care. The effect of vitamin D level on mortality could not be compared with the literature since no pregnant woman died due to the disease during our study period. We think that the absence of mortality and the low need for intensive care in our study are related to the fact that our patients had no comorbidities, their mean age was 29.3 years and all of them were women.

### Limitations

The limitations of our study are the small sample size, the fact that vitamin D levels are not routinely checked in healthy pregnant women, the comparison of vitamin D levels of pregnant women diagnosed with COVID-19 with healthy pregnant women, and the lack of vitamin D levels in outpatient pregnant women with positive COVID-19 RT-PCR test and no indication for hospitalization. In addition, the patients included in the study were from two different hospitals and since the kits of all parameters were not always available in the laboratory for each patient, some parameters of some patients could not be studied during hospitalization or discharge, and only comparisons were made between those with both values.

## CONCLUSION

Vitamin D has become very popular during the pandemic process. However, our study showed that although our patient numbers were not high and we could not reach pregnant women with COVID-19 who were followed up as outpatients, vitamin D level did not have a significant relationship with any of the parameters such as clinical, laboratory findings, severity of the disease and hospitalization periods related to COVID-19. In addition, vitamin D level varies according to geographical location, race and seasons. Therefore, if vitamin D is to be used as an isolated marker in studies, we think that multicenter, high-participant and especially randomized controlled studies will contribute more to the literature.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was carried out with the permission of the Gazi Yaşargil Training and Research Hospital Non-Interventional Clinical Researches Ethics Committee (Date: 27/07/2021 Decision No: E-58146266) and Dicle University Faculty of Medicine Non-interventional Clinical Researches Ethics Committee (Date: 27/05/2021 Decision No: 339).

### Informed Consent

All patients signed and free and informed consent form.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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**Ahmet Değirmenci**

Dr. Ahmet Değirmenci studied at Dicle University Faculty of Medicine between 2005-2011. He graduated from Dicle University Faculty of Medicine in 2011 and received the title of Medical Doctor. He worked as a general practitioner in the provinces of Diyarbakır as part of his compulsory service obligation. In 2017, he started working as a research assistant at Dicle University Department of Obstetric an gynecology, he graduated in 2022 and received the title of expert Medical Doctor (obstetrician and gynecologist). He works as a obstetrician and gynecologist in Ergani Devlet Hastanesi

