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The Relationship Between COVID 19 Infection and Vitamin D Levels

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ABSTRACT

Objective: This study aims to examine the level of vitamin D, wich is an immunomodulator, in Covid-19 patients. **Materials and Methods:** 580 patients with positive Real Time-Polymerase Chain Reaction (RT-PCR, PCR) test were screened from the national health data system. 91 patients whose vitamin D levels were checked recently were included in the study. In addition, 91 people with the same characteristics with negative PCR test were taken as the control group. **Results:** The average age of the Covid 19 patient group was 53.05±16.01, while the control group was 55.32±9.0 years, it was observed 39.6% of the participants were male and 60.4% were female. Vitamin D levels of positive patients, 69.2% (<20 ng / mL) deficiency, 23.1% (20-30 ng / mL) insufficiency, 7.7% (30-149 ng/mL) was found to be optimal and the average vitamin D is 17.61 ng / ml. Control group were found to be 58.2% deficiency, 24.2% insufficiency, 17.6% (30-149) optimal, and the average was 20.75 ng / ml. **Conclusion:** Vitamin D deficiency is more common in Covid 19 patients, and the average of vitamin D is generally lower in Covid 19 patients. Vitamin D supplementation is important in our fight against Covid 19.

Keywords: COVID-19, Low Level, Vitamin D, Prevalence.

COVID 19 Enfeksiyonu ve D Vitamini Düzeyleri Arasındaki İlişki

ÖZ

Amaç: Bu çalışma, Covid-19 hastalarında bir immünomodülatör olan D vitamini düzeyini incelemeyi amaçlamaktadır. **Gereç ve Yöntem:** Aile hekimliği sistemimize kayıtlı Real Time-Polymerase Chain Reaction (RT-PCR, PCR) testi pozitif olan 580 hasta ulusal sağlık veri sisteminden taranmış ve D vitamini düzeyi yakın zamanda kontrol edilen 91 hasta araştırma grubuna dahil edilmiştir. Ayrıca aynı özelliklere sahip PCR testi negatif olan 91 kişi kontrol grubu olarak alındı. **Bulgular:** Covid-19 hasta grubunun yaş ortalaması 53.05±16.01 yıl, kontrol grubunun 55.32±9.00 yıl iken, katılımcıların %39.6'ının erkek, %60.,4'ının kadın olduğu gözlendi. Covid-19 pozitif olan hastaların %69.2'sinde D vitamini eksikliği (<20 ng/mL), %23.1'unda (20-30 ng/ml) D vitamini yetersizliği, %7.7'inde ise (30-149 ng/mL) optimal düzeyde olduğu gözlendi. Ayrıca D vitamini ortalaması da 17.61 ng/mL idi. Kontrol grubunun ise D vitamini düzeyleri %58.2 eksiklik, %24.2 yetersizlik, %17.6 (30-149) optimal ve ortalama 20.75 ng/ml olarak bulundu. **Sonuç:** Covid 19 hastalarında D vitamini eksikliği daha fazla görülmektedir ve genel olarak Covid 19 hastalarında D vitamini ortalaması da daha düşüktür. Covid 19 ile mücadelemizde D vitamini takviyesi önemlidir.

Anahtar Kelimeler: COVID-19, Düşük Seviye, D Vitamini, Yaygınlık.

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INTRODUCTION

Vitamin D has positive effects on immunological mechanisms of many components of natural or adaptive immune system, also provides a healthy mineralized skeletal system and endothelial membrane stability (Medrano et al., 2018). Vitamin D receptors and metabolizing enzymes have been observed in a variety of immune cells. Studies have shown, vitamin D has important biological activities on the both innate and inducible immune system (Vanherwegwn et al., 2017; Sassi et al., 2018), and there are many studies showing the relationship between vitamin D and various infectious diseases and the prevalence and clinical features of some rheumatological diseases (Maertens et al., 2020). Active vitamin D (1-25 (OH) 2 vitamin D) has been shown to be a very effective hormone in inhibiting the proliferation and inducing terminal differentiation of various malignancies (Alptekin, 2017). Vitamin D is protective against respiratory viral infections. Active vitamin D has an antiviral effect and stimulates the release of cathelicidin, affects toll-like receptor counts, and modulates the inflammatory response in viral infection by suppressing Natural Killer Cell (NK) function as well as excessive secretion of proinflammatory cytokines (Teymoori-Rad et al., 2019). Besides immunomodulatory and anti-viral effects, 1-25 (OH) 2 vitamin D specifically acts as a modulator of the renin-angiotensin pathway and reduces angiotensin converting enzyme-2 (ACE-2) receptor expression in the host cell that mediates sarscov-2 infection (Cui et al, 2019). Therefore, it has been suggested that vitamin D supplementation may reduce the risk and severity of COVID-19 infection (Grant et al., 2020; Mendy et al, 2020). The aim of this study is to examine the level of vitamin D in Covid 19 patients compared to control individuals.

MATERIALS AND METHODS

Study type

This case-control study was conducted on Covid-19 Patients Registered with the Family Health Center between April 2020 and July 2020.

Study group

Blood tests from the national health data system (e-Pulse) of 580 patients who were registered in our family medicine system and whose PCR test was positive were scanned. In particular, 91 patients' vitamin D levels examined within 1 month before the diagnosis of Covid19 disease and who did not receive an active vitamin D treatment were identified and included in the study group. In addition, 91 people of the same age, gender, and no symptoms of Covid 19, (fever, joint and muscle pains, cough, weakness, sore throat, headache and dizziness, diarrhea, smell and taste disorder in the last month) whose PCR test was negative, and whose vitamin D levels were examined within the last month, were also selected as the control group. Those whose vitamin D levels were examined for more than one month and those who met the conditions but received vitamin D treatment within the last month were excluded from the study.

Data collect

Vitamin D levels are taken from the national health data system. If, 25 (OH) vitamin D level was under 20 ng / mL, then it's considered as vitamin D deficiency, 20-30 ng / mL level vitamin D named insufficiency and above 30 ng / mL were considered normal (Manson et al., 2016; Fidan et al., 2014).

Statistical analysis

The data were recorded in the SSPS 18.0 package program and statistical analysis was performed. Numerical variables shown as mean, ± median and standard deviation, categorical variables as number (n) and percentage (%). In comparison of categorical variables of the patient and control groups, t test, anova, and chi-square test of significance were used. $P<0.05$ value set as statistically significant.

Ethical considerations

In order to conduct the study, approval was obtained from the Ministry of Health and the Non-Interventional Ethics Committee of the local university (2021/15-01).

RESULTS

Of the patients with Covid 19 and the control group participating in our study, 39.6% were male and 60.4%were female (Table 1). It was observed that the group of patients with Covid 19 ages was especially concentrated over the age of 40. In the control group, it was observed that it was concentrated between the ages of 41-60 (Table 2). When the demographic characteristics of 182 people participated in our study such as age (Table 1) and gender (Table 2) were compared, it was observed that there was no significant difference.

Table 1. Covid 19 patient group and control group gender distribution (n=91).

Sex	Covid 19 patient group		Control group		p
	n	%	n	%	
Male	36	39.6	36	39.6	>0.05
Female	55	60.4	55	60.4	
Total	91	100.0	91	100.0	

Table 2. Covid 19 patient group and control group ages distribution(n=91).

Year	Covid 19 patient group		Control group		p
	n	%	n	%	
21-40	22	24.1	3	3.3	>0.05
41-60	34	37.4	61	67.0	
61>	35	38.5	27	29.7	
Total	91	100.0	91	100.0	

Table 3. Covid 19 and control group vitamin D(n=91).

ng/mL	Covid 19 patient group		Control group		p
	n	%	n	%	
0-20	63	69.2	53	58.2	>0.05
21-29	21	23.1	22	24.2	
30-149	7	7.7	16	17.6	
Total	91	100.0	91	100.0	

In patients with Covid 19, 69.2% of vitamin D levels were detected as (0-20 ng/ml) deficiency (severe deficiency), 23.1% as (21-29 ng/ml) insufficiency (moderate deficiency), 7.7% as 30-149 ng/ml optimal level. In the control group, it was observed that 58.2% of vitamin D levels were 0-20 ng/ml deficiency, 24.2% was 21-29 ng/ml insufficiency, 17.6% was 30-149 ng/ml optimal (Table 3).

The mean vitamin D of the Covid 19 patients participating in the study was 17.61±12.7 ng/mL, while the mean vitamin D of the control group participants was 20.75±11.97 ng/mL. There was no statistically significant difference between the patients with Covid-19 and the control group (p>0.05). But vitamin D levels were found to be 17.83% lower in Covid-19 patients compared to the control group. To summarize, while the average of vitamin D in the community is low or insufficient, vitamin D levels in Covid-19 patients are even lower and at more deficiency levels. However, there was no relationship between increased susceptibility to Covid-19 in those with vitamin D deficiency (p>0.05) (Table 4).

Table 4. Comparison of the vitamin D average of Covid 19 and control group(n=91).

	Covid 19 patient group D vitamin Level		Control Group D vitamin Level		p
	X	SD	X	SD	
Average	17.61	12.70	20.76	11.97	>0.05

X=Mean, **SD**=Standart deviation.

Our multiple comparisons with these data we have found; Vitamin D levels of participants aged 61 and over in the control group showed a positive significant difference at p<0.05 significance level compared to the control group participants aged 41-60. In other words, participants aged 61 and over in this control group give more importance to vitamin D.

DISCUSSION

In our study, there was no statistically significant difference between our study group and the control group with regard to age and gender (p>0.05) (Table 1-2). We found that vitamin D levels in men (mean 20.39±13.33) were higher than in women (mean 18.39±11.76). Studies have also found lower levels of vitamin D in women. While vitamin D levels were sufficient in almost one out of every 6 people in the control group (n=16, 17.6%), this rate was even lower in Covid patients (n=7, 7.7%). According to Bozkaya et al. (2017) they found the rate of vitamin D to be at normal levels in the whole population of 11.3%. Our study also overlapped with this study and we found that this rate (n=182) was 11.53%. Comparing the vitamin level, which is already at low levels in the whole society, between the patient (Covid19 patients) and the healthy group, it may not give clear statistical

results as it may also be a shortcoming of our study. However, we found that vitamin D levels were lower in patients with Covid-19 than in the control group. Vitamin D is a highly discussed and researched vitamin lately. Due to its deficiency, it is now being accepted as a vitamin D deficiency pandemic. There are many studies reporting an increase in the frequency of upper respiratory tract infections in children and adults with vitamin D deficiency. Evidence suggests maintaining a healthy vitamin D level is important in terms of regulating body's immunity. Low serum 25 (OH) D levels are associated with many immune-related diseases, including autoimmune disorders and infectious diseases (Pfotenhauer & Shubrook, 2017). In a study conducted by Martineau et al. (2017) on children, it was found that viral upper respiratory tract infections were observed more frequently in children with low vitamin D. In our study, we observed lower vitamin D in patients with Covid 19 compared to the control group. Pham et al. (2019) reported in a meta-analysis study that vitamin D is protective against respiratory tract infections. Jolliffe et al. (2021) also reviewed 1528 unique studies and found that it had a protective effect, although not very much, in both lower and upper respiratory tract infections. We also say that vitamin D may have a protective effect in respiratory tract infections that may occur in Covid 19 patients and in cytokine storms with its immunomodulatory role. In a study conducted by Sabetta et al. (2010) on 198 healthy adults, it was found that by keeping the vitamin D level above 38 ng / dL, viral upper respiratory tract infections and the number of sick days could be seen 2 times less. In our study, the average vitamin D was 17.61 ng / dL. In other words, it was almost half the value found by Sabetta et al. (2010). Due to the cytokine storm and multiorgan failure that developed in Covid19, the need for intensive care units has also increased and unfortunately, it has forced intensive care conditions in many countries. Studies have also shown that vitamin D improves the duration and prognosis, especially in intensive care(de Haan et al, 2014; Vipul et al., 2017). In fact, Han et al. (2016) Observed that both the length of stay in the intensive care units and the mortality decreased when 36 intubated patients took high doses of vitamin D. They also reported that these patients had low vitamin D levels during their hospitalization in intensive care. According to this study, considering that there may be a need for a ventilator due to problems such as pneumonia after Covid 19, vitamin D supplementation may be beneficial in these patients. In the study performed by Joo et al. (2017) on 805 patients with tuberculosis, it was observed that the rate of vitamin D with 20 ng / dL was 71.7 %. In our study, it was approximately 69.2% in patients with Covid 19. So close values were found. While the deficiency was 72.1% in their control group, it was 58.2% in our control group (Joo et al., 2017). In a study conducted on 128 Hepatitis B (HBV) patients (91 positive HBeAg, 37 negative HBeAg), Chen et al. (2015) found that vitamin D was significantly low in HBeAg positive cases with viral replication. And even protective properties of vitamin D have been reported in preventing HBV and Hepatitis C (HCV) replication and delaying the clinical progression of HBV / HCV-associated liver diseases (Chen et al., 2015; Gutierrez et al., 2014). Shaldoum et al (2020) investigated the effectiveness of intralesional vitamin D injection as an immunotherapy method in the treatment of wart caused by Human Papilloma Virus (HPV) and found that a complete cure was obtained at a rate of 66.7%. Brockman-Schneider et al (2020) showed that it can affect the quality of the antiviral immune response in their study with vitamin D replacement and posterior administration of Rhino virus to intact lung tissues left over from surgical procedures. In another study, the relationship between Human Immunodeficiency Virus (HIV) infection and vitamin D was investigated and it was found that vitamin D positively affected the prognosis (Viard et al., 2011). Eckard et al. (2018), in his study on HIV patients, found that high-dose vitamin D supplementation could help antiretroviral therapy in HIV with immune activation. It is not known whether vitamin D has a similar effect on Corona virus. Xu et al. (2020) state that vitamin D plays a role in the functioning of normal immunity and the appropriate response of adaptive immunity. He states vitamin D also has important role in the fight against this Covid-19 both in the fight of our body and in the formation of adequate post-vaccine antibody response to this pathogen, which treatment is still not found, which we can only fight with mask-distance and vaccine (Xu et al., 2020). Radujkovic et al. (2020) conducted a study on a total of 185 Covid-19 patients, 92 outpatients and 93 inpatients. In their study, they found a statistically significant low level of vitamin D in inpatients. They found that deaths and the need for oxygen support were especially in patients with low vitamin D (Radujkovic et al., 2020). These findings supported our hypothesis. Mohan et al. (2020) report that vitamin D is healthier than other immunomodulators in controlling viral replication and re-establishing the immune balance to prevent cytokine storm. Because other known immunomodulators act like a double-edged knife, and sometimes may weaken the body's fight against Covid 19 by reducing the immunity of the host (Mohan et al., 2020). Mitchell (2020) mentions in his study that epidemics and especially deaths occur in Scandinavian countries with low vitamin D levels and mentions about the benefits of vitamin D supplementation. He even recommends that the elderly population staying in nursing homes should be given vitamin D regularly, especially during this epidemic period (Mitchell. 2020). In our study, the level of vitamin D was low in the patient and control groups, and additional vitamin D is required for the healthy functioning of the defense system. Our study was conducted on a limited number of patients registered in the family health center, which has a limited population. There is a need for new researches that can be done with large case groups to gain more information about the relationship better.

CONCLUSION

Vitamin D is a vitamin that has serious functions and its importance is becoming more and more understood day by day. Today, we understand that vitamin D plays a role in the prevention of autoimmune diseases, diabetes, cardiovascular and muscle disorders as well as cancer. We think that it would be good to give it to the public with the health policies of the country because unfortunately its dietary intake is also insufficient and sometimes it is seen in seasonal deficiencies. In these days when Covid 19 is making a pandemic, we are of the opinion that giving vitamin D, especially those with deficiency, will be beneficial in our fight against this disease.

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Conflict of Interest

The author declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Author Contributions

Plan, design: AD; **Materials and Methods:** AD; **Data analysis and interpretation:** AD; **Writing and corrections:** AD.

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