

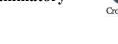
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# A Comprehensive Analysis and Assessment of Vitamin D with Inflammatory

**Biomarkers Levels Among Acute COVID-19 Infected Patients** 



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# Abstract

HE coronavirus disease 2019 (COVID-19) pandemic is only one of several zoonotic illnesses that have caused epidemics over the years that have killed millions of people over the course of millennia. This study included 88 patients with acute COVID-19 infection from Egypt. They were classified in to 3 groups with mild, moderate, and severe COVID-19 manifestation. Patients subjected to full history taking and clinical examination, CT scans of the chest, PCR test for Covid19 and blood sampling for vitamin D and Comprehensive inflammatory markers analysis. The present study reported statistically significant increase of age, dyspnea and respiratory rate (p <0.05) in sever infected groups than mild or moderate groups of COVID-19 patients. Moreover, the primary analysis outcome was significantly associated mortality with reduced hemoglobin levels and elevated values of white blood cells, platelets, D-dimer, LDH, ferritin, blood urea and increased Prothrombin Time (p <0.05). However, insignificant statistical difference was found between the measured serum levels of Vitamin D in patients who recovered from those who died (96.58 $\pm$  38.34 vs 100.75  $\pm$  80.62). This study concluded that COVID-19 severity correlates with multiple inflammatory biomarkers and coagulation factors. While the evidence concerning the therapeutic effect of vitamin D on the outcomes of acute respiratory infections is still controversial but a causal link between level of Vitamin D and the risk of COVID-19 severity and mortality not entirely excluded.

Keywords: Vitamin D, COVID-19, Inflammatory markers, Patients, Mortality.

# **Introduction**

The World Health Organization defines zoonotic illnesses as infections that spread from nonhuman animals to people and can be parasitic, bacterial, fungal, or viral [1]. The following are some frequent instances of zoonotic diseases: fungal (Aspirigeius, cryptococcus and histoplasmosis) [2]. Parasitic protozoa and helminthes (leishmaniasis, hydatidosis, giardiosis, cryptosporidiosis and toxoplasmosis) [3-6]. Viral (rabies, influenza, herpes and yellow fever) [7, 8], and bacterial (staphylococcus, salmonellosis, brucellosis, plaque, and leptospirosis) [9, 10], Animals have been essential to the advancement of human civilization in a variety of spheres, including commerce, transportation, food, and shelter. Because of this, there is now more interaction between people and animals, which makes it easier for these illnesses to spread [11]. Another instance of how a zoonotic virus that is thought to have originated from a live animal market in the Chinese province of Wuhan led to an unanticipated pandemic that impacted the entire world is the severe acute respiratory syndrome coronavirus 2 (Sars-CoV-2) pandemic that occurred in 2019-2020 [12].

Patients diagnosed with coronavirus disease 2019 (COVID-19) typically appear with mild to moderate symptoms and signs depending on organ affection, and the pandemic has placed a serious strain on healthcare facilities [13]. Severe cases, however, may result in problems that swiftly advance to respiratory failure brought on by alveolar injury and acute respiratory distress syndrome (ARDS), which could ultimately result in death [15]. Patients with severe COVID-19 have immediate lung injury, which is characterized by an uncontrolled immunological response in the host that triggers the so-called "cytokine storm," which causes substantial tissue damage and abnormal coagulation [16]. Furthermore, a number of studies have shown that advanced age and co-morbidities such as hypertension, cardiac damage, liver damage, and kidney failure are risk factors for mortality in patients with COVID19 [17]. It follows that prompt and accurate diagnosis is unquestionably crucial. The most effective diagnostics for identifying SARS-CoV-2 were previously thought to be enzyme linked immune-sorbent assay (ELIZA) [18], chest computed tomography (chest-CT) [19] and the gold standard identifying SARS-CoV-2 in COVID-19 for suspicious cases, however, is acknowledged to be RT-qPCR [20].

Current evidence-based studies have also noted that low vitamin D levels are a major risk factor for acute respiratory infections (ARIs), including COVID-19 [21]. Based on investigations conducted at the molecular level, vitamin D and its receptor have been shown to be crucial for both the innate and adaptive immune systems. These studies have shown that vitamin D interferes with most immune system cells, including neutrophils, dendritic cells, B and T lymphocytes, and macrophages [22]. Furthermore, it was discovered that the human body's antibacterial and anti-inflammatory actions are mitigated by vitamin D levels [23]. Studies have looked at inflammatory markers in relation to COVID-19, including LDH, ferritin levels, CRP, procalcitonin, D-dimer, and acute phase response proteins. Higher levels of these markers are linked to a more severe form of the illness and the risk factors that accompany it. Ongoing debate, nevertheless, centers on how inflammatory indicators function in determining the severity of COVID-19 [17]. Even though there are several causes of vitamin D insufficiency, it can quickly and affordably identified and treated. When administering the daily maintenance therapeutic dose of vitamin D, an updated meta-analysis revealed measurable benefits in protection against acute respiratory infections (ARIs) [24]. Therefore, the goal of this work is to measure the serum level of vitamin D and other inflammatory biomarkers in Egyptian patients diagnosed with COVID-19 during the pandemic period and assess the severity of the disease and the clinical outcome of the patients accordingly, given that prescribing vitamin D intake is generally safe, affordable, and accessible.

# **Material and Methods**

### Patients

This study included 88 patients with confirmed COVID-19 were admitted at Alzahraa University Hospital and were referred via the Outpatient clinics of Chest diseases and Complementary medicine, Medical and Scientific Centre of Excellence, National Research Centre during the pandemic period from March 2021 to September 2021 to Al-Azhar University Hospital.

The Cases enrolled in the study were adult patients aged >18 years old on daily vitamin D supplementation 3 months prior to the study and suffering from one or all of the following symptoms: respiratory symptoms (cough, dyspnea, chest tightness), fever  $\geq$  38 or sudden loss of taste and smell. Together with one or all the following conditions within 14 days before symptoms appearance: Direct contact with suspected or confirmed case of Covid19, being a health care worker, having typical imaging findings or positive for SARS-CoV-2 real-time reverse transcriptionpolymerase chain reaction.

The Pregnant or lactating women and subjects with severe underlying diseases, such as advanced malignant tumour and end-stage lung disease were excluded. Also, patients with intestinal malabsorption syndromes including inflammatory bowel disease or patients with chronic liver, kidney diseases, and congestive heart failure were excluded.

#### Study design

The patients were classified according to the disease severity into 3 groups as follows: Mild (30 cases): Symptomatic case with Lymphopenia or Leucopenia but no radiological signs for pneumonia. Moderate (28 cases): Symptomatic case with Lymphopenia or Leucopenia but with radiological signs for pneumonia. Severe (30 cases): Symptomatic cases with RR  $\geq$ 30, SaO<sub>2</sub> < 92 on room air, PaO<sub>2</sub> / fiO<sub>2</sub> ratio <300, chest radiology showing more than 50 % lesion or progressive lesion within 24 to 48 hours.

All patients subjected to full history taking including COVID 19 symptoms (cough, dyspnea, and fever, loss of smell and taste, and diarrhea), comorbidities and direct contact with suspected or confirmed case. In addition to clinical examination (General and Local chest examination), laboratory investigations and Computed Tomography (CT) scans of the chest. All the recovered patients with COVID-19 met the following criteria: having completely resolved symptoms and signs, having significant improvement in pulmonary and extrapulmonary organ function and no longer need for treatment nor supportive care [25].

## **Blood samples**

Venous blood was removed; 2 ml was taken for the whole blood picture, 2 ml was placed in an EDTA tube containing sodium citrate to measure prothrombin time (PT), INR, CRP, and D-dimer, and 3 ml of the blood samples were allowed to clot before the sera were promptly separated for the biochemical parameters [26].

# **Biochemical measurements**

The biochemical parameters were done on the same day, including blood urea, serum creatinine, ALT, AST, ferritin, LDH, by HITACHI auto analyser. (Japan), according to the manufacture's instruction [27]. The serum samples were stored at  $-20^{\circ}$ C after careful labelling till the time of

25(OH)D3 level measurement. Vit-D (1.25 Dihydroxyvitamin D) level measurement was done by Quantitative determination using ELISA technique [28]. These kits were supplied from Elabscience (Texas, USA) with Cat. No: E-EL-0015 and value was expressed as ng / ml. 25(OH)D3 values less than 20 ng/ ml was considered deficient, 20–29 ng/ml was considered insufficient, and adequate levels were considered as at least 30 ng/ ml [29].

# Statistical analysis

After anonymized, the gathered data input onto a personal computer and subjected to statistical analysis. The mean and standard deviation (SD) of the normally distributed data displayed. If not, the interquartile range (IQR) and median are used. Comparatively speaking, categorical data represented by percentages and relative frequencies. ANOVA, or one-way analysis of variance, used to compare more than two means. Additionally, two means compared using the independent samples student "t" test. The study employed the Chi square test to evaluate the correlation between categorical variables. The next step involved computing multiple linear regression analysis to find predictors of both disease severity and death. P-values of less than 0.05 deemed significant for interpreting the findings [30].

# **Results**

# Relation between range of vitamin concentration and number of persons

The measurement of Vit-D (Dihydroxy vitamin D) levels in all tested persons was done by quantitative determination using ELISA technique. The most prevalent levels are from 50 to 100 ng/mL (40 samples) followed by concentration of 100 to 150 ng/mL (37 samples) and lowest vit D concentration ranged from 200 to 250 ng/mL (2 samples) followed by concentration of 150 to 200 ng/mL (4 samples) (**Figure 1**).

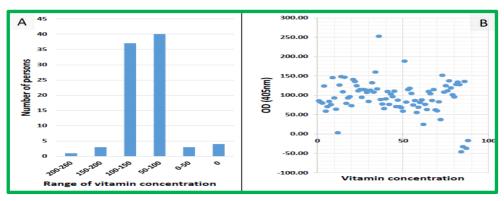


Fig. 1. Relation between range of vitamin concentration and number of persons

# Comparison between disease severity and studied variables

The present study enrolled 88 Patients with COVID-19 infection. The subject's characteristics as well as their clinical symptoms and the association between disease severity and studied variables summarized. Patients were categorized into mild, moderate, and severe cases. The age was significantly different between the 3 groups (p = 0.001) using ANOVA test as patients with severe infection were significantly older (58.13±11.94) compared to patients with moderate (55.89±12.16) and mild disease (46.60±13.06). Males and females were matched with no significant difference in the distribution between cases. PCR test for COVID-19 was found to be positive in 66.7% of patients with mild symptoms with respect to 71.4 % and 80 % in patients with moderate and severe disease respectively (Table 1).

Among patients with mild disease, 26.7% of the patients were smokers compared to only 14.3% and 16.7% of patients with moderate and severe Covid 19 respectively. The majority of the cases suffered from cough while only a minority of them complained from GIT symptoms, but none were present with any neurological complaints. However, dyspnea was more observed in patients with moderate (89.3%) and severe (90%) disease compared to patients with mild (60%) COVID-19 (p = 0.005, using Chi square test). Respiratory rate was high in patients with moderate (24.04±3.17) and severe (26.14±6.03) compared to patients with mild  $(21.63\pm3.61)$  Covid19 manifestations (p = 0.001, using ANOVA test), but no significant statistical difference was noted in body temperature, heart rate nor the blood pressure between the different groups of patients (Table 1).

Variables		Mild group (30 cases)	Moderate group (28 cases)	Severe group (30 cases)	Test	p-value
Age		46.60±13.06	55.89±12.16	58.13±11.94	7.257	0.001*
Gender	Male Female	17(56.7%) 13(43.3%)	14(50.0%) 14(50.0%)	17(56.7%) 13(43.3%)	0.34	0.840
Smoking		8(26.7%)	4(14.3%)	5(16.7%)	1.63	0.440
Cough		29(96.7%)	27(96.4%)	28(93.3%)	0.47	0.780
Dyspnea		18(60.0%)	25(89.3%)	27(90.0%)	10.69	0.005**
GIT sympt	oms	10(33.3%)	10 (35.7%)	10 (35.7%)	0.048	0.970
• •	al symptoms	0(0.0%)	0(0.0%)	0(0.0%)	-	-
Positive PC		20(66.7%)	20(71.4%)	24(80.0%)	1.37	0.500
Temperatu		37.54±1.65	37.39±0.52	37.44±0.85	0.145	0.865
Heart rate		90.80±8.39	90.36±10.70	88.50±14.46	0.337	0.715
Blood	Systolic	126.67±16.88	122.50±14.80	125.67±17.36	0.504	0.606
Pressure	Diastolic	80.33±11.59	75.36±8.38	76.67±9.59	1.960	0.147
Respirator	y rate	21.63±3.61	24.04±3.17	26.14±6.03	7.554	0.001*
Hemoglobin (g/dl)		13.16±1.59	12.08±1.63	12.33±2.15	2.876	0.062
WBCs x 10		$7.60 \pm 5.98$	$6.05 \pm 2.90$	$10.0 \pm 6.32$	5.114	0.008*
Lymphocy	tes (IQR)	$1.53 \pm 1.30$	1.70 ±0.95	$1.06 \pm 1.03$	0.783	0.460
Neutrophil		4.90 ±4.70	$4.50 \pm 2.55$	$3.75 \pm 5.93$	0.335	0.716
N/L ratio	· - /	0.31±0.45	$30 \pm 0.25$	0.27±0.62	2.761	0.069
Platelets x	10 <sup>3</sup>	288.0±146.50	201.50±110.25	319.00±182.50	0.749	0.476
D-dimer (n	ng/I)	0.40±0.23	$1.20{\pm}0.88$	1.20±0.85	13.701	<1.001*
LDH (mg/d	ll)	196.5±19.1	234.0±134.75	479.0±334.5	13.933	<1.001*
Ferritin (ng/ml)		131.0±98.1	361.0±158.25	498.0±197.1	4.591	0.013*
CRP (mg/l)		7.0±0.65	$14.0 \pm 8.0$	$24.0 \pm 11.9$	6.093	0.003*
ALT (U/ml)		20.5±18.50	31.0±23.75	39.0±37.0	4.289	0.017*
AST (U/ml)		$27.0 \pm 13.25$	$42.0 \pm 32.50$	$36.0\pm30.0$	5.054	0.008*
Urea (mg/d	I)	25.0±20.0	40.5±34.25	51.0±42.00	4.976	0.009*
Creatinine		$0.75 \pm 0.43$	$0.80{\pm}0.30$	1.0±0.65	0.728	0.486
PT (Second		12.30±0.27	13.80±1.42	15.52±2.50	27.884	<1.001*
Vitamin D	(Pg/ml)	95.75±44.58)	93.66 ±39.17	101.58±59.59	0.166	0.847
Mortality		0(0.0%)	0(0.0%)	11(36.6%)	13.42	0.001**

GIT: Gastrointestinal; PCR: Polymerase chain reaction; WBCs: While blood cells; L/N: lymphocyte/neutrophils ratio; IQR: Interquartile range; IDH: Lactate dehydrogenase; CRP: C-reactive protein; ALT: Alanine transaminase; AST: Aspartate transaminase; PT: prothrombin Time; \* indicate significant differences ( $p \le 0.05$ ).

# Comparison between mortality and other variables

Regarding the blood count, white blood cells were elevated in severe cases compared to mild and moderate cases (p-value = 0.008, using Chi square test). While there were no reported significant statistical differences between the studied groups with respect to their hemoglobin levels, nor their lymphocytes, neutrophiles and platelets counts. Also, serum creatinine was normal in all cases but other laboratory markers such as D-dimer, LDH, Ferritin, CRP, ALT, AST, Urea and PT were markedly elevated in patients with moderate and severe infection compared to patients with mild Covid-19. Serum vitamin levels exhibited insignificant difference between the three groups of cases and was adequate in all groups ( $95.75\pm44.58$  vs  $93.66\pm39.17$ vs  $101.58\pm59.59$ ) for mild, moderate, and severe Sars CoV 2 infection respectively (p=0.847). Seventyseven patients completely recovered from covid 19 while 11 patients died from severe disease complications. Their disease characteristics and studied variables (**Table 2**).

Va	ariables	Improved and survived (n=77)	Arrested and died (n=11)	Test	p-value
Age		52.24±13.24	62.18±10.16	2.38	0.019*
	Male	42(54.5%)	6(54.5%)	0.001	1.00
Gender	Female	35(45.5%)	5(45.5%)	0.001	1.00
Smoking		16(20.8%)	1(9.1%)	0.84	0.35
Cough		73(94.8%)	11(100.0%)	0.59	0.43
Dyspnea		60(77.9%)	10(90.9%)	0.99	0.31
GIT sympto	ms	25 (32.5%)	5(45.5%)	0.72	0.39
Neurological	l symptoms	0(0.0%)	0(0.0%)	-	-
Positive PCI	ર	56(72.7%)	8(72.7%)	0.001	1.00
Temperatur	e	37.43±1.13	37.64±0.89	0.59	0.55
Heart rate		90.55±10.53	85.09±16.00	1.49	0.13
Blood	Systolic	124.15±15.41	130.90±21.65	1.28	0.20
Pressure	Diastolic	77.40±9.92	78.18±11.67	0.23	0.81
Respiratory	rate	23.81±4.71	24.60±5.56	0.48	0.63
Hemoglobin	(g/dl)	12.69±1.80	11.38±1.81	2.26	0.026*
WBCs x 10 <sup>3</sup>	(median(IQR)	6.80±5.0	11.80±5.90	3.25	0.002*
Lymphocyte	es (IQR)	$1.50 \pm 1.10$	0.90±1.0	1.01	0.31
Neutrophils	(IQR)	4.50±3.55	3.10±9.95	0.06	0.94
L/N ratio (IC	QR)	0.31±0.41	0.23±1.02	0.53	0.59
Platelets x 1	0 <sup>3</sup>	237.0±133.0	400.50±149.0	3.19	0.002*
D-dimer (mg	g/I)	$0.60 \pm 0.80$	$1.30 \pm 0.90$	2.08	0.041*
LDH (mg/dl	)	$230.0 \pm 156.0$	499.0 ±356.0	4.17	< 0.001*
Ferritin (ng/	/ml)	$253.0 \pm 102.7$	579.0 ±225.8	2.45	0.016*
CRP (mg/l)		$12.0 \pm 1.0$	$20.0 \pm 21.0$	0.07	0.94
ALT (U/ml)		$27.0 \pm 18.0$	31.50 ±21.30	1.69	0.093
AST (U/ml)		$33.0 \pm 26.0$	33.50 ±23.25	1.45	0.15
Urea (mg/dl)	)	$36.0 \pm 32.0$	$48.50 \pm 15$	2.46	0.016*
Creatinine (	mg/dl)	$0.80 \pm 0.40$	1.0 ±0.62	0.14	0.88
PT (Second)		13.57±1.76	16.00±3.12	3.81	<0.001*
Vitamin D (	Pg/ml)	96.58 ±38.34	100.75 ±80.62	0.25	0.79

 TABLE 2. Comparison between mortality and other variables

GIT: Gastrointestinal; PCR: Polymerase chain reaction; WBCs: While blood cells; L/N: lymphocyte/neutrophils ratio; IQR: Interquartile range; IDH: Lactate dehydrogenase; CRP: C-reactive protein; ALT: Alanine transaminase; AST: Aspartate transaminase; PT: prothrombin Time; \*Significant differences using t-test at  $p \le 0.05$ . indicate significant differences ( $p \le 0.05$ ).

# Analysis of disease severity

Mortality was significantly associated with older age, reduced hemoglobin levels, elevated values of white blood cells, platelets, D-dimer, LDH, ferritin, blood urea, and increased PT. Similarly, no statistically significant difference was observed between the measured serum levels of Vitamin D3 in patients who recovered from those who died (96.58  $\pm$  38.34 vs 100.75  $\pm$  80.62) (**Table 3**).

Covid 19 found to be positive in 66.7% of patients

with mild symptoms with respect to 71.4 % and 80 % in patients with moderate and severe disease

respectively. Patients with severe infection were

significantly older (58.13±11.94) compared to

patients with moderate (55.89±12.16) and mild

disease  $(46.60\pm13.06)$  and were present with a high respiratory rate  $(26.14\pm6.03)$  compared to patients

with moderate  $(24.04\pm3.17)$  and mild  $(21.63\pm3.61)$ 

statistically significant difference between patients

concerning cough and GIT symptoms however;

dyspnea was more prevalent in patients with

Regarding symptoms, we did not note any

TABLE 3. Analysis of disease severity	y and mortality	y with sig	ificant single variables
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	Disease severity		Mor	ality
	Beta	P-value	Beta	P-value
Age	-0.016	0.873	0.117	0.279
Dyspnea	0.070	0.544	-	-
RR	0.207	0.082	-	-
WBCs	-0.003	0.967	0.206	0.025*
D-dimer	0.098	0.282	-2.261	0.027*
LDH	0.244	0.005*	0.317	0.001*
Ferritin	0.014	0.884	0.10	0.91
CRP	0.206	0.018*	-	-
ALT	-0.060	0.583	-	-
AST	0.140	0.194	-	-
Urea	-0.035	0.718	0.11	0.27
РТ	0.577	< 0.001*	0.27	0.004*
Hemoglobin			-0.251	0.004*
Platelets			0.395	< 0.001*

RR: Respiratory rate; WBCs: White blood cells; LDH: Lactate dehydrogenase; CRP: C-reactive protein; ALT: Alanine transaminase; AST: Aspartate transaminase; PT: prothrombin Time; \* indicate statistical significance at P-value<0.05

### Discussion

Infection with SARS-CoV-2 virus can affect different organs and cause variable symptoms that may even persist for many months after the acute infection. More than 85 % of the patients are present with mild to moderate forms of the disease with complete resolution after adequate treatment and care; however, severe manifestations of the disease accompanied by serious complications and high risk of mortality particularly in vulnerable patients [31]. Given the novel nature of the virus, various recommendations. and guidelines the for management of the disease proposed along with anticovid vaccines [32]. Many medications also repurposed to treat this highly contagious viral infection, but the cornerstone of management approaches essentially based on the reinforcement of the immune system [33]. Not surprisingly, recent research during the pandemic investigated the link between serum 25 (OH) D3 concentrations and the course of SARS-CoV-2 and most studies agree that vitamin D deficiency related to a poor prognosis of the disease [34]. Nevertheless, literature data on the effectiveness of vitamin D supplementation to reduce the severity of Covid19 infection remain inconsistent [35]. Hence, we sought to assess the clinical outcomes of Covid19 infection and the prognosis of patients who were on daily vitamin D supplementation prior to enrolment in this current study. In fact, in our cohort of patients, serum vitamin D levels were adequate, and no significant statistical difference found between the studied groups of patients as shown in table 1. PCR test for

moderate (89.3%) and severe (90%) disease compared to patients with mild (60%) Covid19. On the contrary, none of our patients complained from any neurological symptoms, which often observed in around 80 % of the patients affected by SARS-CoV-2 virus [36]. Implying that vitamin D supplementation may also have neuroprotective

manifestations.

2 virus [36]. Implying that vitamin D supplementation may also have neuroprotective effects, which have already been shown, possibly as a result of vitamin D's function in preventing inflammatory cells from entering the nervous system and inducing the release of neurotrophic cytokines, which encourage the differentiation, growth, and development of neurons [37]. Noteworthy, we also measured the ration between the Neutrophil to lymphocyte (NLR), a marker for disease severity and systemic inflammation based on evidence highlighted by a recent meta-analysis which showed that NLR values were increased in severe covid 19 representing a predictor for Intensive Care admission [38]. In the present study, we observed that the NLR was not elevated in all the 3 groups of the patients in agreement with results found by Maghbooli et al. who examined the therapeutic effects of vitamin D on the prognosis of patients infected with Covid 19 [39]. Our finding is also consistent with clinical trials during which patients with Covid19 who received high doses of vitamin D had mild to moderate disease with improved clinical outcomes and therefore decreasing the need for critical care [40].

These data can be explained mostly because vitamin D supplementation improve the immune function and protect against tissue damage via antiinflammatory actions on T-lymphocytes possibly also leading to few mortalities [41]. Interestingly, various publications described those low levels of serum 25 (OH) D3 was associated with increased severity and mortality [42]. Accordingly, even though we couldn't find any significant difference in the vitamin D levels between those who recovered from the disease from those who didn't survive the severity of their infection caused by Sars-Cov-2 virus similarly to the work done by Alsegai et al who evaluated vitamin D levels in critically ill adult patients with covid-19 [43]. An additional important finding in the present study is the incidence of mortality observed among our patients concurring with recent studies that showed no association between circulating serum levels of vitamin D and fatality rates [44]. On the contrary, a retrospective study concluded oral supplementation of 25 (OH) D3 could be responsible of reducing the risk of mortality in patients with Covid19 by 70% [45]. In line with various data on the inverse correlation between mortality and vitamin D supplementation during the pandemic [46].

However, based on the above-mentioned results, a causal link between the circulating levels of Vitamin D and the risk of Covid 19 severity and mortality could not entirely excluded particularly with extensive evidence that described the therapeutic effect of vitamin D in regulation of both the adaptive and the innate immune response against bacterial and viral infections. [23]. [Furthermore, mortality due to Covid 19 can also attributed to other confounding factors such as age, sex, and comorbidities [17]. [Indeed, our assessment of this cohort of Egyptian patients revealed that severe disease was significantly associated with older age and increased levels of inflammatory markers such as white blood cells, D-dimer, LDH, Ferritin and CRP. Additionally in the current study, linear regression analysis revealed that severe disease significantly correlated with increased LDH, CRP and PT. Moreover, our results showed that in addition to elevated LDH and PT, increased white blood cells and platelets, high D-dimer values and reduced

hemoglobin levels were all significantly associated with mortality similar with earlier findings that showed significant correlation between the disease severity and these inflammatory markers recommended for monitoring of the disease prognosis [47]. Supplementing with vitamin D3 raises serum concentrations of both total vitamin D and 25(OH)D, with variations based on baseline 25(OH)D. This indicates that 25-hydroxylation of vitamin D3 is more effective when serum 25(OH) D is low [48]. It is possible to conjecture that the inconsistent outcomes attributed to the nonhomogeneous participant groups, varied duration, inconsistent study criteria, and variability in measurement performance. However, given that our study was single-center and focused on patients with severe COVID-19 symptoms who had previously taken vitamin D as a preventive measure, the reported rates of severity and mortality may skewed. As such, the results of this work interpreted with some limitations in mind.

# Conclusions

Overall, the current study's results indicate that while a number of inflammatory indicators can predict the risk of severe COVID-19 infection and mortality, the exact role of vitamin D is still unknown. In order to further understand the mechanisms that could lead to the evidence-based prescription of vitamin D as a therapeutic supplement to enhance the prognosis of acute respiratory viral infections, future multicenter collaboration and study are required with varying severity symptoms of Covid-19.

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# Conflicts of interest

The authors declare that there is no conflict of interest.

### Ethical considerations

Prior to the study, all subjects signed a written informed and illustrative consent form. The Ethics Committee of the Ministry of Health and Population, Training and Research Sector, examined and authorized this study. The study was assigned approval number 22-2020/17. Prior to the study, all subjects signed a written informed and illustrative consent form.

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تحليل وتقييم مستويات فيتامين د والمؤشرات الحيوية للالتهابات بين المرضى المصابين بعدوى. كوفيد-19 الحادة

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إن جائحة مرض فيروس كورونا 2019 (كوفيد-19) ليس سوى واحد من الأمراض المشتركة العديدة وتسببت في أوبئة على مر السنين أودت بحياة ملايين الأشخاص على مدار آلاف السنين. تم إجراء هذا البحث لتقييم تأثير مستوى فيتامين د على العديد من مؤشرات الالتهاب المختلفة على النتائج السريرية و التنبؤات المتوقعة في مرضى المصابين بفيروس الكوفيد 19 شملت هذه الدراسة 88 مريضًا مصابًا بعدوى كوفيد-19 الحادة من مصر. وتم تصنيفهم إلى 3 مجموعات تعاني من أعراض كوفيد-19 الخفيفة والمتوسطة والشديدة. تم إخضاع المرضى لأخذ التاريخ الكامل والفحص السريري، والأشعة المقطعية للصدر، واختبار PCR لـ Covid19 وأخذ عينات من الدم لفيتامين د وتحليل علامات الالتهاب الشامل. أبلغت الدراسة 81 مريضًا مصابًا بعدوى كوفيد-19 أوخذ عينات من الدم لفيتامين د وتحليل علامات (P) في المجموعات المصابة بشدة مقارنة بالمجموعات الخفيفة أو المعتدلة من مرضى كوفيد-19. علاوة على الالتهاب الشامل. أبلغت الدراسة الحالية عن زيادة ذات دلالة إحصائية في العمر وضيق التنفس ومعدل التنفس ( P ذلك، كانت نتيجة التحليل الأولي هي الوفيات المرتبطة بشكل كبير بانخفاض مستويات الهيموجلوبين وارتفاع قيم خلايا (P) في المجموعات المصابة بشدة مقارنة بالمجموعات الخفيفة أو المعتدلة من مرضى كوفيد-19. علاوة على الدم البيضاء والصفائح الدواسة الحالية عن زيادة ذات دلالة إحصائية في العمر وضيق التنفس ومعدل التنفس ( P ذلك، كانت نتيجة التحليل الأولي هي الوفيات المرتبطة بشكل كبير بانخفاض مستويات الهيموجلوبين وارتفاع قيم خلايا الذين تعافوا من أولنك الذين ماتوا (BOB لي المونيتين واليوريا في الدم وزيادة زمن البروثر ومبين ( P دالذين تعافوا من أولنك الذين ماتوا (BOB لي 2001 لي 2001). وخلصت هذه الدراسة إلى أن شدة كوفيد-19 ترتبط بالعدين ماتوا (BOB لي 400 لي علين مستوى فيتامين د المقاس في المصل لدى المرضى كوفيد-19 الذين تعافوا من أولنك الدي التفاسي الحرابي وعوام الذين المرضى وخليت عافوا من أولنك الذين ماتوا (BOB لي 400 لي الذين تعافوا من أولنك الذين ماتوا (BOB لي 400 لي 400

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