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Level of serum 25(OH) vitamin D among hospitalized COVID-19 patients in Iraq, Diwaniyah city

Bushra Gatea Abbas
M.B.Ch.B. F.I.C.M.S/FM. Membership of clinical nutrition. Afak Primary Health Care Sector. Al Diwaniyah, Iraq

Nawal Mehdi Al Khalidi
M.B.Ch.B. C.A.B.M F.I.C.I.S (Gastroenterlogy and Hepatology). Consultant in gastroenterology and hepatology. Gastroentrology and Hepatology Hospital in Medical City. Baghdad, Iraq

Ali Haleem Jasim
M.B.Ch.B. C.A.B.H.S/Community medicine. Membership of clinical nutrition. Ministry of health/Minister´s office

***Abstract*---**Introduction: COVID-19 is an emerging viral infection whose pathogenic mechanisms are not well understood. Interestingly, Vitamin D deficiency and COVID-19 share prevalence patterns for hypertension, diabetes, obesity, advanced age, and male sex. Vitamin D deficiency can contribute to our understanding of COVID-19 health disparities. Patients and methods: a cross sectional study involving 100 adult hospitalized patients with positive PCR for COVID-19 at Diwaniyah teaching Hospital / Shiffaa center, Diwaniyah, Iraq, during a period of 3 months. The serum 25 OH-D level was measured and Vitamin D deficiency, defined as a 25(OH) D level < 20 ng/mL, and insufficiency define as a 25(OH)D level 30-20 ng/mL. History of some other underlying health diseases (diabetes mellitus, hypertension, hypothyroidism and gastro esophageal reflux disease) was taken directly from the patients. The data was analyzed using SPSS version 26 and the study aimed to measure serum vitamin D level among COVID-19 patients. Result: The mean ± SD age was 38.8±13.7 years ranging between 18- 67 years. The mean±SD of 25(OH)D levels was 20.2±16 ng/mL. Vitamin D deficiency was present in 58 patients and vit D insufficiency was found in 25 patients. Those with vitamin D deficiency did not differ from those who were sufficient (vitamin D ≥ 20 ng/mL) in terms of age, gender or comorbidities. Conclusion: low 25(OH) vitamin D levels were highly prevalent among hospitalized COVID-19 patients Vitamin D supplementation should be considered an adjuvant therapy for COVID-19.

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Introduction

Vitamin D appears to be essential not only for 'healthy bones' but also for many other organs and tissues[1]. However, low Vitamin D status seems to be a global problem: it was estimated that about 1 billon humans could have Vitamin D deficiency or insufficiency[2]. Many factors can contribute to high prevalence of low Vitamin D, eg, modern sedentary life style (less and less time outside in the sunlight), obesity and air pollution (particularly, in large cities) that reduces the amount of solar UV radiation reaching the humans, dietary habits (decreased consumption of diary and sea fish), avoidance of sunlight even during leisure time, use of sunscreen, cultural habits (eg, clothing style) in some populations, as well as low rates of Vitamin D supplementation and absence of food fortification with Vitamin D programs in many countries[3, 4].

Undoubtedly, the COVID-19 pandemic is a significant burden on global health systems as well as a major issue for global economics. It was Originated in China by the end of 2019, a new disease caused by a novel coronavirus named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) continues to spread rapidly around the world and still is a huge challenge for many countries[5]. Indeed, the COVID-19 virus is found to be more dangerous for elderly people, especially for those who have comorbidities, in particular, arterial hypertension, obesity, diabetes, cardiovascular or cerebrovascular diseases, as well as for ethnic minority populations with darker skin, since these patients have higher risk of severe COVID-19 and also higher mortality rates[4-6]. Interestingly, these mentioned COVID-19 risk groups could also be considered as risk groups for Vitamin D deficiency[7, 8].Epidemiological studies of the past showed inverse relationships between Vitamin D status and certain clinical events, e.i lower vitamin D levels are associated with higher risk of developing Acute respiratory distress syndrome, heart failure and sepsis; the latter conditions are also known to increase risk for severe COVID-19 and death from COVID-19[9, 10].

Aim of the Study

To measure serum vitamin D level among COVID-19 patients and prevalence of some other underlying health diseases (diabetes mellitus, hypertension, hypothyroidism and gastro esophageal reflux disease) with it association with vitamin D level.

Patients & Methods

A cross sectional study involving adult hospitalized patients at Diwaniyah teaching Hospital / Shiffaa center, Diwaniyah, Iraq. During a period of 3 months, a total of 100 hospitalized patients with moderate and sever COVID-19 infection and positive by real-time polymerase chain reaction (PCR) test results and age above 18 years were included, while those who are taking Vitamin D3 supplements or having taken them in the last 6 months were excluded. As the major circulating form of Vit D is 25 OH-D and it is currently accepted as the best marker of Vitamin D status[11], the serum 25 OH-D level was measured, Vitamin D deficiency, defined as a 25(OH)D level < 20 ng/mL, Vitamin D insufficiency,

defined as a 25(OH)D level between 30-20 ng/mL [12].History of some other underlying health diseases (diabetes mellitus, hypertension, hypothyroidism and gastro esophageal reflux disease) was taken directly from the patients. The data was analyzed using SPSS version 26.

Result:

A total of 100 patients were included in this study, the mean ± SD age was 38.8±13.7 years ranging between 18- 67 years. The distribution of 25(OH)D levels is shown in figure 1. The mean ± SD of Vit D was 20.2 ±16 ng/mL. The median 25(OH)D level of those with 25(OH)D < 20 ng/mL was 9 (IQR: 5–13) ng/mL.

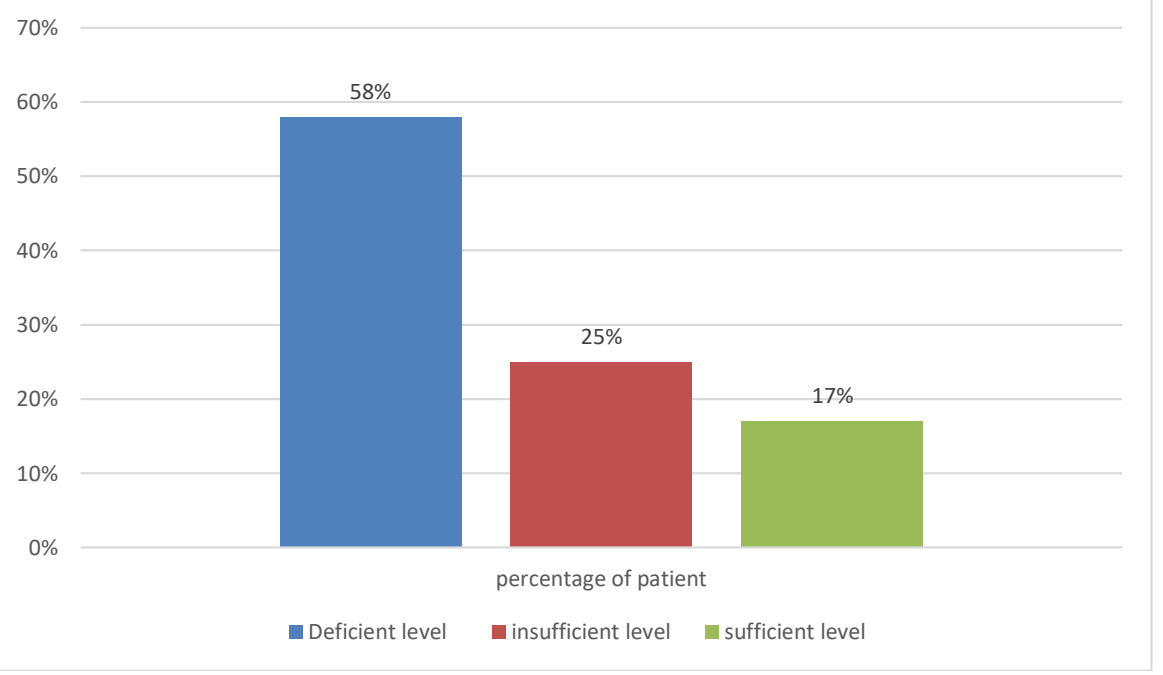

Figure -1- Distribution of Vitamin D level among studied patients.

Those with vitamin D deficiency did not differ from those who had sufficient vitamin D (vitamin D ≥ 20 ng/mL) in terms of age, gender or comorbidities.

Table -1- Relation of vitamin D level with age, gender and comorbidity

Variables		Vitamin D level		Total	P value
		<20ng/ml	≥20ng/ml		
Age in years	18-39	31(57.4%)	23(42.6%)	54	0.6**
	40-59	22(57.9%)	16(42.1%)	38	
	≥60	5(62.5%)	3(37.5%)	8	
	Mean ±SD	38.2± 14.3	39.7 ±13	38.8±13.7	
Gender	Female	35(66%)	18(34%)	53	0.084*
	Male	23(48.9%)	24(51.1%)	47	
Smoking	Positive	16(59.3%)	11(40.7%)	27	0.87*

	Negative	42(57.5%)	31(42.5%)	73	
DM	Positive	10(66.7%)	5(33.3%)	15	0.46*
	negative	48(56.5%)	37(43.5%)	85	
Hypertension	Positive	17(58.6%)	12(41.4%)	29	0.93*
	negative	41(57.7%)	30(42.3%)	71	
Hypothyroidism	Positive	3(60%)	2(40%)	5	0.92**
	negative	55(57.9%)	40(42.1%)	95	
GERD	Positive	9(56.3%)	7(43.8%)	16	0.87*
	negative	49(58.3%)	35(41.7%)	84	
Total		58	42	100	

*Chi-square test,**Student T test, significant ≤0.05.

Discussion

Vitamin D's regulation of immune function. Vitamin D levels, vitamin D metabolites, and vitamin D receptor polymorphisms play a role in immune function via actions on T lymphocyte recruitment and activation as well as modulation of innate immune responses such as induction of antimicrobial peptides and other antimicrobial effector mechanisms[13, 14]. Vitamin D has also been shown to reduce proinflammatory cytokines, thereby reducing inflammation. Vitamin D has also been shown to reduce proinflammatory cytokines, thereby reducing inflammation[15]. And as the main goal of this across sectional study was to determine the vitamin D deficiency among COVID -19 patients in addition to determine the effect of age, gender and other comorbidity on the level of vitamin D. in this study 58% of patients had vitamin D deficiency, with mean serum vitamin D level (20.2±16 ng/ml). These results agreed with a recent study conducted in *Louisiana State* which found that 57.1% of COVID-19 patients had Vitamin D deficiency [16], also this study shown that: only 17% of patients had sufficient vitamin D and this result in line with a study done in Iran: that shown only 19.4% of COVID19 patients had sufficient vitamin D[17]. In fact, there is promising evidence of the connection between vitamin D status and risk of incident COVID-19 infection. For example, Kaufman et al [18] investigated the likelihood of a positive test for COVID-19 in a national clinical laboratory database of 191 779 patients and found that SARS-CoV-2 positivity is strongly and inversely associated with circulating 25(OH)D levels, a relationship that persists across latitudes, races/ethnicities, both sexes, and age ranges. The result was in line with that of a single-center, retrospective cohort study by Meltzer et al [19]showing that deficient vitamin D status was associated with an increased risk of testing positive for COVID-19 (relative risk, 1.77; 95% CI, 1.12-2.81) after adjustment in a multivariate analysis compared with likely sufficient vitamin D status.

In a new large racially and ethnically diverse cohort study shown that there was a significant independent inverse dose-response relationship between increasing continuous 25(OH)D concentrations (from 15 to 60 ng/mL) and decreasing probability of COVID-19-related hospitalization (from 24.1 to 18.7%, p=0.009) and mortality (from 10.4 to 5.7%, p=0.001)[20]. Also a pre-clinical studies demonstrate that 25(OH)D stimulates immune and respiratory epithelial cells to secrete cathelicidin, an anti-microbial peptide that clears respiratory pathogens. 25(OH)D

also initiates adaptive immunity to dampen down pro-inflammatory cytokines ("cytokine storm") leading to adverse COVID-19 outcomes[21, 22]. The current study shown no significant association of vit D level with age, gender and comorbidity, this similar to Italy study that observed absence of a correlation between comorbidity (DM, COPD, HT, IHD, CKD) and 25(OH)vitamin D level[23],also similar to a result for a study done in USA [24]. The study limitations, which consist mainly in being monocentric, like the vast majority of those already published, and in the limited sample size. Also this study is cross-sectional by design; therefore, causal relationship could not be determined with certainty.

Conclusion

Very low 25(OH)vitamin D levels were highly prevalent among hospitalized COVID-19 patients, but low 25(OH)Vitamin D levels were not associated with comorbidity variables. Whether 25(OH) vitamin D adequacy may prevent COVID-19 infection or influence clinical outcomes needs to be assessed by adequately sized and designed population-based studies and intervention trials, respectively, which could be very relevant in the unfortunate occurrence of new outbreaks.

Ethical Clearance: Taken from the Arab board of health specializations.
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Conflict of Interest: No conflict of interest

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