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Assessment of Serum Vitamin D Level in Patients with COVID-19 Infection

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Abstract

Background: Given the pandemic crisis of COVID-19 infection and the controversy that surround the different lines of treatment which range from simple multivitamins to the very expensive antiviral drugs which at most of times lack the solid evidence of efficacy, many studies are needed to determine the influence of such myriad of this unlimited drugs and specifically to determine if this supplementary medicines -vitamins and minerals-does actually have a role in management of these patients or just represent unwanted polypharmacy. This study is intended to determine the contribution of vitamin D deficiency to the severity of Covid-19 infection.

Aim of Study: To determine the association between serum vitamin D level and the severity of covid-19 infection.

Patients and Methods: A prospective study including eighty threepatients was conducted in Chest and Clinical Pathology Departments in Bab El-Sha'aria and Al-Hussin Hospitals, Al-Azhar University during the period from January 2021 to June 2021. Serum vitamin D3 level was assessed ineighty three patients with COVID-19 infection of variable severity, diagnosed based on the integrated clinical, laboratory, and CT chest radiological data.

Results: This study include83patientswith mean age of 48.4±17.8 including 26 (31.3%) males and 57 (68.7%) females. Regarding the severity of covid-19 infection; 35 (42.2%) patients was suffering from non pneumonic Covid-19 infection,mild pneumonic covid-19 infection was present in 11 (13.3%) patients, covid-19 pneumonia of moderate intensity was present in 18 (21.7%) patients and severe covid-19 pneumonia was present in 19 (22.9%) patients. As regard the vitamin D3 it was sufficient in 20 (24.1%) patients, insufficient in 37 (44.6%) patients and deficient in 26 (31.3%) patients. CRP ranges from 4 to 96 with mean of 23.3±22.9. Correlation between the serum level of vitamin D and the severity of covid-19 infection was done.

Conclusion: This study conclude that there is no association between the severity of covid-19 infection and the serum level of vitamin D. But because ofits common insufficiency and deficiency among population and patients with covid-19 infection and its importance for the immune system and the modulation of inflammatory response, vitamin D could be given in the daily recommended doses as a supplementary measure, however further studies are warranted to determine if larger doses of vitamin D could alter the disease course of covid-19 infection.

Key Words: *Vitamin D – COVID-19 infection.*

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Introduction

VITAMIN D is a asteroid fat soluble hormone that is mainly produced endogenously through the effects of ultraviolet rays exerted over its precursors beneath the skin, also it could be obtained exogenously from the fortified food as it is mostly present in a small amount in the natural food [1]. Vitamin D plays an important role in the regulation of immune defense mechanisms that help to guard the respiratory system against a broad spectrum of infections [2], it could increase the level of T regulatory lymphocytes which possess an important role against uncontrolled inflammation that is induced by viral infection and such cellswas found to be low in patients with Covid-19 infection [3], also the vitamin D can induce the production of cathelicidin and β2-defensins, a pluripotent peptides that possessa significant antiviral effects and enhance the mucosal defense mechanisms [4]. Manyclinical studies reported that the incidence of epidemic influenza and lower respiratory tract infection was higher among patients with hypovitaminosis D [5] and a recent meta-analysis found that there is 64% increased risk of community acquired pneumonia in subjects with hypovitaminosis D less than 20ng/ml [6]. In addition, the vitamin D have an important regulatory role in the coagulation cascade and the lower levels of vitamin D was found to be associated with an increased propensity for thrombosis which represent one of the major concerns among patients with covid-19 infection [7]. Higher levels of inflammatory markers and subsequent induction of cytokine storm was

also found to be associated with hypovitaminosis D [8]. Vitamin D deficiency is a common health problem among populations [9] and many epidemiological studies have found a lower risk of Covid-19 infection [10] and its consequences like thrombotic events and cytokine storm [8] with adequate levels of serum vitamin D. Given the lack of potential curative antiviral drugs against the Covid-19 infection, the attention was concentrated for the preventive measures such as vitamin D supplementation as there is cumulative evidence that proper vitamin D level seems to be associated with a lower incidence of respiratory tract infection [5].

Aim of the work:

To determine the association between serum vitamin D level and the severity of covid-19 infection.

Patients and Methods

A prospective study including eighty three patients was conducted in Chest and Clinical Pathology Departments in Bab El-Sha'aria and Al-Hussin Hospitals, Al-Azhar University during the period from January 2021 to June 2021. Serum vitamin D3 level was assessed in all patients with non-pneumonic and pneumonic COVID-19 infection of variable severity, diagnosed based on the integrated clinical, laboratory, and CT chest radiological data.

All patients after giving a written consent were subjected to the following:

Clinical history and examination.

Laboratory tests: (CBC, CRP, LDH, S. Ferritin, D-dimer, liver and renal functions and PCR for covid-19).

Imaging: CXR and HRCT chest.

Inclusion criteria:

All patients with suspicious symptoms of COVID-19 infection.

Exclusion criteria include:

- Patients known to suffer from chronic illnesses including diabetes mellitus, renal, hepatic, cardiovascular, respiratory and endocrinal diseases.
- Pregnant females.

Procedure:

This assay was intended for the quantitative determination of total serum 25-hydroxyvitamin D(25(OH)D) in patients with Covid-19 infection using electrochemilum inescence binding assay on cobase 411 immunoassay analyzers, test number 1500: Application code number 166.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 24. For descriptive statistics: The mean ± SD was used for quantitative variables while the number and percentage were used for qualitative variables. For analytic statistics: Kruskal Wills test: Was used when comparing between more than two means (for abnormal distributed data), Chi-square test: Was used when comparing between non-parametric data. A one-way analysis of variance (ANOVA): When comparing between more than two means (for normal distributed data). The statistical methods were verified, assuming a significant level of $p<0.05$ and a highly significant level of $p<0.001$.

Results

This study include 83 patients with COVID-19 infection based on their clinical laboratory and radiological features, with age range of 13-80 years and mean age of 48.4±17.8, there was 26 (31.3%) males and 57 (68.7%) females (Table 1).

Table (1): General characteristics of the studied patients.

Variables	Studied patients (N = 83)	
Age (years):		
Mean ±SD	48.4±17.8	
Min - Max	13-80	
Sex:		
Male	26	31.3%
Female	57	68.7%

Pneumonic infiltrates was absent in 35 (42.2%) patients while mild pneumonia was present in 11 (13.3%) patients, moderate pneumonia was present in 18 (21.7%) patients and severe pneumonia was present in 19 (22.9%) patients (Table 3).

In all of the studied patients, serum vitamin D level ranges from 6.8-48.6ng/ml with mean of 24.5±8.6 (Table 2), it was sufficient in 20 (24.1%) patients, insufficient in 37 (44.6%) deficient in 26 (31.3%) patients (Table 3).

Table (2): Description of laboratory data in all studied patients.

Variables	Minimum	Maximum	Mean	Std. Deviation
CRP	4	96	23.3	22.9
Vit. D	6.8	48.6	24.5	8.6

Table (3): Description of pneumonia and vitamin D status in all studied patients.

Variables	Studied patients (N=83)	
Pneumonia:		
No	35	42.2%
Yes	48	57.8%
Severity:		
Non-pneumonic	35	42.2%
Mild pneumonic	11	13.3%
Moderate pneumonic	18	21.7%
Severe pneumonic	19	22.9%
Vit. D status:		
Deficient	26	31.3%
Insufficient	37	44.6%
Sufficient	20	24.1 %

Among patients with non-pneumonic covid-19 infection serum vitamin D level was sufficient in 12 (60%) of patients, insufficient in 14 (37.8%) and deficient in 9 (34.6%). In patients with mild pneumonic covid-19 infection, serum vitamin D was sufficient in 1 patient (5%), insufficient in 6 patients (16.2%) and deficient in 4 patients (15.4%). In patients with moderate pneumonia serum vitamin D level was sufficient in 6 (30%), insufficient in 7 (18.9%), and deficient in 5 (19.2%). In patients with severe pneumonia serum vitamin D level was sufficient in 1 (5%), insufficient in 10 (27%), and deficient in 8 (30.8%) (Table 4) with no statistically significant difference.

Table (4): Relation between Vit. D status and severity of COVID-19 infection.

Variables	Vitamin D status						Stat. test	*p*-value
	Deficient (n=26)		Insufficient (n=37)		Sufficient (n=20)			
COVID-19 severity:								
Non-pneumonic	9	34.6%	14	37.8%	12	60%	$X^2 = 8.01$	0.238 NS
Mild pneumonic	4	15.4%	6	16.2%	1	5%		
Moderate pneumonic	5	19.2%	7	18.9%	6	30%		
Severe pneumonic	8	30.8%	10	27%	1	5%		

In the current study the CRP ranges from 4 to 96 with mean of 23.3±22.9 among the studied population (Table 2) and there was no statistically significant difference when the vitamin D status was correlated with the level of the CRP (Table 5).

Table (5): Relation between vitamin D status and CRP.

Variables	Vitamin D status			Stat. test	*p*-value
	Deficient (n=26)	Insufficient (n=37)	Sufficient (n=20)		
CRP (mg/L):					
Median	12	12.4	12.5	KW = 2.26	0.323 NS
IQR	11.7-13.2	11.7-13.9	12-13.3		

Discussion

Up till now there is no global standard classification for the severity of covid-19 infection, but for the purpose of this study which include eighty three patients with covid-19 infection, the patients were categorized according to the presence or absence of pneumonic infiltrates in CT chest as patients with non-pneumonic Covid-19 infection and patients with pneumonic covid-19 infection,the later were further stratified into those with mild, moderate and severe pneumonic covid-19 infection based on clinical and radiological data.

Patients with radiological infiltrates but without tachypnea nor desaturation was considered as mild pneumonic covid-19 while patients with SpO2 >93% and respiratory rate less than 30bpm was considered as moderate pneumonic covid-19 ,patients with SpO2 ≤93% at rest or respiratory rate more than thirty per minute was considered as severe pneumonic covid-19 infection, and this is in accordance with the case definition adopted in china **[11]**.

The major bulk of vitamin D is formed endogenously through exposure of the skin to the ultra-

violet rays [12]. Inside the body hydroxylation in the liver and kidneys is a must to give the biologically active and measurable form of vitamin D which is the vitamin D3 (25-hydroxyvitamin D (25(OH)D) [13], its biological half-life is two to three weeks and its concentration in the serum is usually more than that of vitamin D2 by many folds, vitamin D2 that is mainly supplied by the fortified food, have a much shorter half-life and is usually immeasurable [14].

There is no international consensus regarding the normal level of vitamin D3 but there is wide agreement that vitamin D deficiency is defined as a serum level of vitamin D3 (25-hydroxyvitamin D (25(OH)D) less than 20ng/ml [15] and an insufficient vitamin D3 is determined when the serum level ranging from 21-30ng/ml [16].

This is in agreement with the study performed with Alireza Davoudi [17] who found that sufficient level of vitamin D was not protective from adverse clinical outcomes in patients with covid 19 infection and also in line with the study performed in the northern Italy hospital that found no association between vitamin D and covid-19 [18].

In clear contrast to the current study, are the studies performed by Javier Mariani et al., [19] and Hiwot Yisak et al., [20] which suggest an association between vitamin D deficiency and the severity of covid 19 infection.

The C reactive protein (CRP) is an acute phase reactant protein, its synthesis is usually triggered by the increased levels of inflammatory cytokines particularly IL-6 and TNF, the higher levels of CRP was associated with the cytokine storm that is contributed to the sever pneumonia and multiple organ failure [21]. This is in contrast with the study performed with Anshul Jain [22] who found that the level of inflammatory markers was higher among covid-19 infected patients who suffer from vitamin Ddeficiency, the dissociation between this finding and the current study may be explained by the fact that comorbiditiescould enhance the severity of inflammatory markers which was not taken into account in the mentioned study, while patients with comorbidities was excluded from the current study. E Kenneth [8] and Mustafa [23] have found that there was an association betweenvitamin D deficiency and higher levels of CRP, the lack of correlation with the present study may be attributed to the fact that cases of non-pneumonic covid-19 (42.2%) and mild pneumonia (13.3%) was higher represented while cases of moderate intensity (21.7%) and sever pneumonia (22.9%) were less represented in the current study (Table 3).

Despite randomized trials and meta-analysis have been shown that adequate supplementation with vitamin D have a defensive role against respiratory tract infections but in regard to covid-19, there is still controversy as some retrospective studies demonstrated an association between vitamin D deficiency and severity of COVID-19 infection, while other studies did not find any association when confusing variables are adjusted [24]. Therefore larger studies are needed to evaluate the association between vitamin D level and the severity of covid-19 infection.

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تقييم مستوى فيتامين د
فى المرضى المصابين بفيروس كورونا المستجد

ارتبط ظهور جائحة كورونا بالجدل الكبير حول الكثير من العقاقير الطبية التى تستخدم فى علاج فيروس كورونا والتى تتفاوت من الفيتامينات والمعادن إلى مضادات الفيروسات والتى تفتقر فى مجملها إلى الدلالات الطبية الكافية على فعاليتها ومدى إحتياج المريض إليها ومن هنا كانت الحاجة إلى هذه الدراسة لتقييم مدى ارتباط مستوى فيتامين د فى الدم بشدة الإصابة بفيروس كورونا المستجد وقد اشتمل هذا البحث على ٨٣ مريضاً من المصابين بفيروس كورونا المستجد منهم ٣٥ مريضاً لا يعانون من إصابات رئوية بينما كان هناك ٤٨ مريضاً يعانون من إصابات رئوية متفاوتة الشدة منهم ١١ مريض بالتهاب رئوى بسيط و ١٨ مريض بالتهاب رئوى متوسط الشدة و ١٩ مريض بالتهاب رئوى شديد ولم تكن هناك دلالة ذات قيمة إحصائية عند مقارنة مستوى فيتامين د فى الدم بمختلف مستويات الإصابة من الشدة. و قد دلت هذه الدراسة على عدم وجود ارتباط وثيق بين نقص فيتامين د وبين شدة الإصابة بفيروس كورونا المستجد إلا أنه نظراً لأهمية فيتامين د فى تنظيم عمل جهاز المناعة ونظراً للنقص الشائع فى مستوى فيتامين د بين كثير من المرضى فإنه يوصى باستخدام فيتا مين د بالجرعات اليومية المقررة للحفاظ على الصحة العامة.