Vitamin D Level and Severity of COVID-19 Patients in North Sinai Governorate, A Clinical Prospective Study

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ABSTRACT

Background: COVID-19, defined as coronavirus disease 2019, is a widespread illness that happened due to the emergent infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that induced a severe health concern with its outbreak. **Aim:** To measure the serum Vitamin D level in North Sinai Governorate cases infected by coronavirus-19 and correlate its level with clinical, laboratory biomarkers, severity and prognosis of the disease. **Patients and methods:** This prospective research has been performed on fifty Egyptian cases who were selected from cases attending the inpatient of North Sinai Hospitals (North Sinai Governorate), Egypt. All cases were found to be infected with coronavirus -19. **Results:** Mean serum vitamin D (Vit. D) was 24.53 ±8.93. According to prognosis, thirty-one (sixty-two percent) cases were discharged and nineteen (thirty eight percent) died. There was significant positive correlation between Vitamin. D and severity of coronavirus-19. Mean O_2 saturation on admission was 85±7. According to clinical symptoms, fifty (hundred percent) cases had fever, sore throat, cough, arthralgia, myalgia, eight (sixteen percent) cases had diarrhea, twenty-one (forty-two percent) cases had abdominal pain, three (six percent) cases had vomiting and forty-five (ninety percent) cases had shortness of breath. **Conclusion:** This study demonstrated that there was a correlation between severity of coronavirus-19 and Vit. D. Further prospective studies with larger scales are necessary for confirming our results.
Key words: Vitamin D, Severe acute respiratory syndrome coronavirus 2, Coronavirus-19

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a widespread illness that was a result of the emergent infection of SARS-CoV-2, which has caused a severe health concern with its outbreak [1]. In cases with moderate symptoms, recovery was typically reported following one week. At the same time, progressive respiratory failure may develop in severe cases due to alveolar damage, this may quickly progress to acute respiratory distress syndrome (ARDS) and cause mortality [2].

Evaluation of the severity and predicting the prognosis of coronavirus-19 using certain indicators, including lactate dehydrogenase (LDH), hypersensitive cardiac troponin I (hs-cTnI), creatinine (CR), aspartate aminotransferase (AST), has been identified in research [3]. Furthermore, several researches have elaborated and identified the potential value of coagulation markers, such as D-dimer (DD) and prothrombin time (PT) in predicting the outcome and prognosis of coronavirus -19 cases [4].

Vit. D is crucial for modulating the immune response to infections [5]. The potential function of Vit. D in reducing the severity of coronavirus-19 in hospitalized cases was discovered in the meta-analysis results. However, additional data from randomized controlled trials is required to substantiate its impacts on mortality

[6]. Vitamin D is synthesized with cholesterol when the epidermis is exposed to sunlight. The energy for Vit. D formation is provided by the sun's ultraviolet B (UVB) radiation, which hits cholesterol in the skin cells [7].

Thrombotic complications frequently occur in cases with coronavirus-19. More than half of cases having severe illness have been discovered to have increased levels of DD. Interestingly, the regulation of thrombotic pathways is also influenced by Vit. D, and a deficiency of this vitamin is correlated with an increase in thrombotic episodes [8]. Theoretically, Vit. D improve and prevent coronavirus-19 sides effects. It has the potential to regulate the innate and adaptive cellular immunity, the physical barriers, and the renin-angiotensin system (RAS), [9,10].

Objective of the research was to measure the serum Vit. D level in North Sinai Governorate cases infected by coronavirus -19 and correlate its level with clinical, laboratory biomarkers, severity, and prognosis of the disease

PATIENTS AND METHODS

This prospective research has been carried out on fifty Egyptian cases who were selected from cases attending the inpatient of North Sinai Hospitals (North Sinai Governorate), Egypt. All cases were found to be

infected with coronavirus-19 from 1 September 2020 to 20 July 2021.

Inclusion criteria: The following criteria were fulfilled by all cases that were confirmed to have coronavirus-19 infection: Positive for severe acute respiratory syndrome coronavirus 2 real-time reverse transcription-polymerase chain reaction (+ ve for RT- PCR) and having suggestive clinical symptoms and imaging findings.

Exclusion criteria: cases with chronic kidney disease (Serum creatinine >3 mg/dl) and cases with cirrhotic liver (Serum Albumin less than 3.5 gm/dl).

METHODS
All patients were exposed to the following: Case history, laboratory investigation including DD and ferritin: Done by enzyme linked immunosorbent assay (E.L.I.S.A). The normal range Male: 20–250 mg/dl// Female :10–120 mg/dl and radiological investigation (Computed tomography (CT) chest finding (assessing the case by CO-RADs).

25-OH vitamin D determination: 25-OH vitamin D determination was done by enzyme linked immunosorbent assay kit, which was supplied from Eagle Biosciences, Inc. (20A Northwest Blvd., Suite 112, Nashua, NH 03063, England).

Ethical consecrations:
All subjects declared a written consent that they agree to participate in the research. The research was accepted and reviewed by the Ethical Committee of Environmental Studies Institute/Environmental Medical Science (Al-Arish University). The purpose of this study was to perform research on humans in compliance with the Declaration of Helsinki; the code of ethics of the World Medical Association.

Statistical analysis
SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA) has been utilized to collect, tabulate, and perform statistical analyses of all data. Frequencies and percentages have been used for presenting qualitative information. Quantitative data have been presented as mean ± standard deviation (SD). Correlations were analyzed using the Spearman rank. P-value of ≤ 0.05 was considered significant.

RESULTS
According to personal history, the mean of age was 59.26±16.6 (Table 1).

Table (1): Shows personal history in the examined group

	Examined Group No (50)
Age (years), Mean± SD	59.26±16.6
BMI (kg/m^2), Mean± SD	28.9±6.98
Sex	
Male	29(58%)
Female	21 (42%)
Smoking Habits	0(0%)

BMI: body mass index

According to clinical symptoms, all the cases had fever, sore throat, cough, arthralgia, and myalgia, while 90% of cases had shortness of breath (Table 2).

Table (2): Shows Clinical Symptoms in the examined group

	Examined Group No (50)
Fever	50(100%)
Sore throat	50(100%)
Cough	50(100%)
Arthralgia	50(100%)
Myalgia	50(100%)
Diarrhea	8(16%)
Abdominal Pain	21(42%)
Vomiting	3(6%)
Shortness Of Breath	45(90%)

According to the inflammatory markers, the mean CRP was 43.5±13.6, the mean ESR was 53.25±29.02, the mean D. Dimer was 0.88±0.34 and the mean Ferritin was 323.5±231.2. (Table 4).

Table (3): Demonstrates inflammatory marker in the examined group

	Examined Group No (50)
CRP (mg/dL), Mean± SD	43.5±3.6
ESR (mm/hr.), Mean± SD	53.25±9.02
D. Dimer, Mean± SD	0.88±0.14
Ferritin (ng/mL), Mean± SD	323.5±31.2

CRP: C-reactive protein. ESR: Erythrocyte Sedimentation Rate.

According to serum vitamin D, the mean was 24.53 ±8.93 (Table 4).

Table (4): Shows serum vitamin D and O_2 saturation on admission in the examined group

	Examined Group No (50)
Serum Vit. D (ng/ml), Mean± SD	24.53 ±4.93
O₂ saturation (%), Mean± SD	85±7

According to prognosis, thirty-one cases were discharged and nineteen died (Table 5).

Table (5): Shows prognosis in the examined group

		Examined Group No (50)
Prognosis	Discharge	31 (62%)
	Died	19 (38%)

According to table 6, significant positive correlation was observed between severity of covid 19 and Vit. D (Table 6).

Table (6): Correlation between severity of coronavirus-19 and Vit. D.

		Vit. D ng/ml
Severity of covid 19	**r**	0.588
	P value	0.001

r: Pearson correlation

Test Result Variables	Area	Cutoff value	Sensitivity	Specificity	PPV (%)	NPV (%)	Std. Error	Asymptotic Sig.	Lower Bound	Upper Bound
Vit D	.720	16.4	48.9%	100%	100	11.11	.129	.205	.467	.973

At cutoff value 16.4 Vit D had sensitivity of 48.9%, specificity of 100%, PPV of 100% and NPV of 11.11% with no significance.
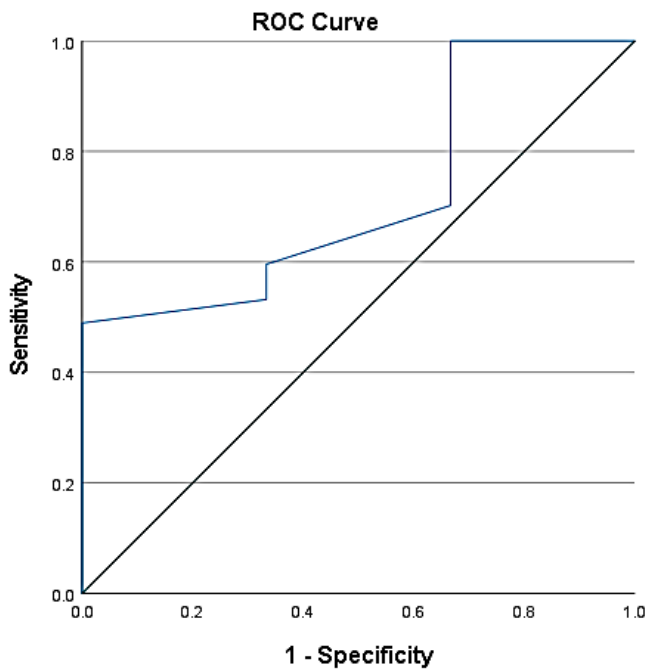
Figure (1): ROC curve for Vit D in prediction of Severity of COVID-19.

DISCUSSION

According to personal history, the mean of age was 59.26±16.6, the mean of BMI was 28.9±6.98 and twenty-nine (fifty-eight percent) of research population were men while twenty-one (forty-two percent) were women.

Ben-Eltriki *et al*. [11] that objected to understand the correlation among elevated inflammatory and cardiac biomarkers and Vit. D deficiency, conducted a meta-analysis that involved 24 observational studies involving 3637 subjects. The cases' average age was 61.1 years.

Also, **Campi** *et al*. [12] objected to prospectively examine, in a good, distinguished cohort of consecutive coronavirus-19 cases admission to their coronavirus-19 hospital, correlation among 25-hydroxy Vit. D levels at hospital admission and related mortality during hospitalization and coronavirus -19 severity. The research involved 361 subjects (two hundred six non-severe acute respiratory syndrome coronavirus 2 infected controls, fifty-two mildly-symptomatic coronavirus-19 cases, one hundred three severely-symptomatic coronavirus-19 cases) with 25-hydroxy vitamin D measurement. The authors reported that the average age of the cases was 66.70 years.

According to inflammatory marker, the mean of CRP was 43.5±13.6, the mean of ESR was 53.25±29.02, the mean of DD was 0.88±0.34 and the mean of ferritin was 323.5±231.2.

According to clinical symptoms fifty (hundred percent) cases had fever, sore throat, cough, arthralgia, myalgia, eight (sixteen percent) cases had diarrhea, twenty-one (forty-two percent) cases had abdominal pain, three (six percent) cases had vomiting, and forty-five (ninety percent) cases had shortness of breath.

Our results are supported with **Huang** *et al*. [13], who initially recorded the clinical symptoms at the onset of illness in cases with coronavirus -19 were, where the most prevalent symptom was fever (ninety-eight percent), then cough (seventy-six percent), fatigue or muscle pain (forty-four percent), dyspnea (fifty-five percent), headache (eight percent), sputum production (twenty-eight percent), hemoptysis (five percent), and diarrhea (three percent).

Furthermore, **Heightman** *et al*. [14] found that the clinical symptoms of their involved cases were fever, sore throat, arthralgia, myalgia, diarrhea, abdominal pain, cough, and vomiting. Moreover, **Weng** *et al*. [15] reported that clinical symptoms of their involved cases were fever, sore throat, cough, arthralgia, myalgia, diarrhea, abdominal pain, and vomiting.

Guan *et al*. [16] observed that the most prevalent pain symptoms are headache (13.6%), sore throat (13.9%), and myalgia or arthralgia (14.9%). In addition to respiratory symptoms, patients with coronavirus-19 frequently complain of pain symptoms, abdominal pain, such as headaches, chest pain, myalgia or arthralgia, and sore throats.

According to serum vitamin D, the mean was 24.53 ±8.93. Regarding O_2 saturation on admission, the mean was 85±7. According to prognosis, there were thirty-one (sixty-two percent) cases who were discharged and nineteen (thirty eight percent) died. Significant positive correlation was observed among severity of covid 19 and vit. D.

Ye *et al*. [17] aimed to observe the association among coronavirus -19 infection, its clinical case characteristics, and its severity and serum 25-hydroxy vitamin D (25(OH)D) level. A case-control study was conducted to compare rates of the serum 25-hydroxy vitamin D levels and vitamin D deficiency (VDD) among eighty healthy controls and sixty-two cases diagnosed with coronavirus-19. Severe/critical coronavirus-19 patients were significantly older and had greater percentages of comorbidity (renal failure) comparing to mild cases. The concentration of serum 25-hydroxy vitamin D within serum in healthy control was higher than in coronavirus-19 cases and mild patients showed the greatest 25-hydroxy vitamin D level in comparison to severe/critical patients. Additionally, significantly greeter rates of Vit. D deficiency were observed in coronavirus -19 patients (41.9%) comparing to healthy controls (11.1%), and Vit. D deficiency was the greatest in severe/critical cases (eighty percent), in comparison to mild cases (thirty-six percent). Statistically significant correlation persisted even following controlling for comorbidities and demographics. A potential threshold of 25-hydroxy Vit. D (41.19 nmol/L) to protect against coronavirus -19 had been determined.

Nielsen *et al*. [18] discovered the correlation among vitamin D status and coronavirus-19 severity utilizing information from Danish nation-wide health registers, stored blood samples from the national biobank, and the coronaviru19 surveillance database. They concluded that low levels of 25-hydroxy vitamin D were correlated with a greater risk of severe coronavirus -19.

Ben-Eltriki *et al*. [11] who demonstrated that low vitamin D status was statistically correlated with greater risk of developing severe coronavirus-19 pneumonia (RR: 1.50; 95% CI, 1.10–2.05), greater risk of mortality (RR, 1.60 (95% CI, 1.10–2.32). Coronavirus-19 cases with less vitamin D levels have cardiovascular diseases and higher prevalence of hypertension, peak DD levels and abnormally high serum troponin, and C-reactive protein and raised interleukin-6 than those with serum 25-hydroxy vitamin D levels equal thirty or more nanograms

per milliliter. The variation between our findings and theirs may be due to different definitions of vitamin D deficiency and of COVID-19 severity. Another important source to this contradiction is timing of vitamin D measurements in relation to the test. Future rigorous prospective studies, using a standardized definition of vitamin D deficiency, insufficiency and sufficiency will be essential.

CONCLUSION
We conclude that, no correlation is observed among severity of coronavirus-19 and levels of vitamin D. Further prospective researches with larger scales for confirming our finding.

DECLARATIONS
- **Funding:** No fund**.**
- **Availability of data and material:** Available.
- **Conflicts of interest:** No conflicts of interest.
- **Competing interests:** None.

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