

Correlation of Vitamin D with Inflammatory Markers in COVID-19 Patient

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Abstract: *Vitamin D in COVID-19 has brought great interest as Vitamin D has been used to treat various other viral infections. So Vitamin D has been used on trial basis to treat the novel corona virus.*

Keywords: Vitamin D, COVID-19

1. Introduction

COVID-19 caused by the severe Acute Respiratory Syndrome Corona Virus 2 (sars-cov-2) often produces severe lower respiratory symptoms and has caused more than 745, 000 deaths worldwide.

Clinically, patients with COVID-19 showed respiratory symptoms that were very similar to other respiratory viral infections. They were also characterized by ground glass opacity in lung x-ray. one challenge in halting this pandemic is the absence of evidence demonstrating effective pharmacologic interventions to prevent covid-19. Vitamin D treatment has been identified as potential strategy to prevent or treat COVID-19.

Vitamin-D treatment has been found to decrease other viral respiratory infections especially in patients with vitamin d deficiency. There is a body of epidemiological and clinical evidence showing that vitamin d can reduce lung injuries through several mechanisms, including inducing the antimicrobial peptides, reducing the concentrations of pro-inflammatory cytokines and increasing the anti-inflammatory cytokines. Not many studies regarding Vitamin D levels in COVID-19 has been done. The present study was conducted to measure levels of Vitamin-D at the time of diagnosis of COVID-19 and correlate with severity of COVID-19, at the time of admission. Hence the need for study.

2. Objectives of the study

To measure levels of Vitamin-D at the time of diagnosis of COVID-19 and correlate with severity of COVID-19, at the time of admission.

3. Method of Data collection

Study design: A cross sectional study was conducted where Patients Admitted at Father Muller Medical College Hospital with diagnosis of COVID-19.

Sample size: 100

Methodology: In the present cross sectional study, 100 consecutive adult COVID-19 patients hospitalized in an tertiary care hospital were enrolled from March to April 2021. 25 (OH) Vitamin D serum levels were assessed 48 h since hospital admission and categorized into: normal (≥ 30

ng/mL), insufficient ($<30\text{--}\geq 20$ ng/mL), moderately deficient ($<20\text{--}\geq 10$ ng/mL), severely deficient (<10 ng/mL).

Lab investigations conducted were Serum Ferritin, Serum LDH, D-DIMER, Vitamin-D

Inclusion criteria:

- 1) Adult with RT-PCR Positive Report.
- 2) Age: 18 years and above

Exclusion criteria:

- 1) Children below 18 years of age
- 2) Patients with pre-existing lung disease
- 3) Patients who have received chemotherapy.

Statistical analysis: Data Entry will be done using Microsoft excel 2013 and analysis done using SPSS V 16. Qualitative data were expressed in frequencies and percentages and Quantitative data in mean and standard deviation. Pearson correlation was used to find the significant correlation between two groups. Bar diagrams and pie chart were used to represent the data. p value of <0.05 was considered statistically significant.

4. Results

In the present study the mean age of the study population was 48.58 ± 16.53 years. 20% belong to 21-30 years age group, 15% were in 31-40 years age group, 14% were in 41-50 years age group, 21% were in 51-60 years age group and 30% belong to >60 years age group.

Distribution based on gender shows, 68% were male and 32% were female. Based on co-morbidities 34% had diabetes and 30% had Hypertension. 24% had history of smoking.

Distribution based on lab parameters shows the mean Neutrophil count was 80.43 ± 3.16 , Mean lymphocyte count was 13.16 ± 1.47 , Mean NLR ratio was 6.19 ± 0.77 , Mean CRP was 244.82 ± 103.59 , Mean D-Dimer levels were 1509.87 ± 670.61 , Mean Ferritin levels were 719.58 ± 439.33 , mean IL-6 levels were 873.02 ± 680.95 .

The prevalence of 25 (OH) vitamin D insufficiency, moderate deficiency and severe deficiency was 13%, 22% and 54%, respectively. The mean Vitamin D levels in the present study was 15.50 ± 11.06 .

The mean CT Severity score in the present study was 14.57 ± 7.35 .

Association between CT severity and Laboratory parameters show a significant correlation between D-Dimer levels ($r=0.46$, $p<0.001$), Serum ferritin ($r=0.47$, $p<0.001^*$), IL-6 ($r=0.43$, $p<0.001^*$).

The present study didn't find a significant correlation observed between CT severity score and Vitamin D levels ($r=0.03$, $p=0.75$).

In the present study, in hospital mortality was 45%.25 (OH) Vitamin D deficiency (<20 ng/mL) was not associated with COVID-19 clinical features and outcomes. Unexpectedly, after adjusting for major confounders, a significant positive association between increasing 25 (OH) vitamin D levels and in-hospital mortality (on a continuous logarithmic scale, odds ratio = 1.73 [95% CI, 1.11 to 2.69]; $P = .016$) was observed.

5. Discussion

The present study was conducted to measure levels of Vitamin-D at the time of diagnosis of COVID-19 and correlate with severity of COVID-19, at the time of admission.

Association of levels of Vitamin D in relation to general parameters:

In the present study the mean age of the patients was observed to be 48.58 ± 16.53 years, and it was observed that there was a significant association between vitamin D deficiency and advancing age and this observation was in consonance with the observations made by Carpagano et al.,¹ Radujkovic et al.,²

The prevalence of 25 (OH) vitamin D insufficiency, moderate deficiency and severe deficiency was 13%, 22% and 54%, respectively. The mean Vitamin D levels in the present study was 15.50 ± 11.06

It was observed that majority of the patients who were hospitalized were observed to have low levels of Vitamin D. a similar observation was done in the study done by Radujkovic A et al.,² In a study conducted by D'avalio et al.,³ they have observed that the Vitamin D levels were significantly lower in people who were tested positive for COVID-19, when compared to general population. In a recently done meta-analysis by Munshi et al.,⁴ it was debated that, the levels of Vitamin D can be used as a prognostic indicator to assess the severity of COVID-19, but it was always quite debatable to decide the cut off values of Vitamin D levels.

Associations of Vitamin D in relation to inflammatory markers:

Vitamin D interferes with the functioning of immune system and the cells mediating it like macrophages, T lymphocytes, dendritic cells, monocytes and macrophages.6 IL-1 β and TNF α are the key activators for the secretion of the IL-6⁷

Association between CT severity and Laboratory parameters show a significant correlation between D-Dimer levels ($r=0.46$, $p<0.001$), Serum ferritin ($r=0.47$, $p<0.001^*$), IL-6 ($r=0.43$, $p<0.001^*$).

In Carpagano et al.,¹ it was observed that the inflammatory markers could be taken as independent predictors for the severity of COVID-19, whereas in the present study the inflammatory markers that are shown to have an association with vitamin D deficiency were Ferritin, AST, Globulin, CRP and D-dimers. But a clear relationship between all the inflammatory markers has not been observed in relation with the Vitamin D and the association to be established as seen in meta-analysis, we may need to do larger studies. A similar case work up scenario has been observed in the study done by Ricci et al.,⁸

But in the larger study done by Latz et al.,⁹ they opined that an independent association between a blood type and the independent inflammatory markers. Vitamin D inhibits the adaptive immune system and promotes the innate immune system, which thus promotes anti inflammatory responses.¹⁰

Thus, in support with the extensive studies, a workup of inflammatory markers and vitamin D together can be considered for assessing the severity of COVID-19.

CT severity

The present study didn't find a significant correlation observed between CT severity score and Vitamin D levels ($r=0.03$, $p=0.75$). In the study done by Ricci et al.,⁸ they have also observed that the severity of CT is having a significant association with the levels of CT.

Vitamin D and status of alive or dead NS

In the present study, in hospital mortality was 45%.25 (OH) Vitamin D deficiency (<20 ng/mL) was not associated with COVID-19 clinical features and outcomes. Unexpectedly, after adjusting for major confounders, a significant positive association between increasing 25 (OH) vitamin D levels and in-hospital mortality (on a continuous logarithmic scale, odds ratio = 1.73 [95% CI, 1.11 to 2.69]; $P = .016$) was observed.

6. Conclusion

Very low 25 (OH) vitamin D levels were highly prevalent and suggestive of deficiency among our hospitalized severe COVID-19 patients, but low 25 (OH) vitamin D levels were not associated with outcome variables. Whether 25 (OH) vitamin D adequacy may influence clinical outcomes in COVID-19 and the unexpected correlation between higher 25 (OH) vitamin D levels and mortality require further investigations by large intervention trials.

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Table 1

	Minimum	Maximum	Mean	SD
Age	19	83	48.58	16.53
Neutrophils	75	85	80.43	3.17
Lymphocytes	11	15	13.16	1.48
NLR Ratio	5	7.7	6.20	0.77
IL 6	23	2093	873.02	680.95
CRP	40	445	244.82	103.59
D Dimer	206	2471	1509.87	670.62
Ferritin	39	1488	719.58	439.33
CT SEVERITY	3	24	14.57	7.35
Vitamin D levels	6.1	50	15.51	11.06

