Original Research Article

Correlations between level of vitamin D serum and disease severity COVID-19

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ABSTRACT

Background: Corona virus disease (COVID-19) Was a respiratory disease. Severity of the disease was related to inflammation process. SCAP scoring system can be used to asses COVID-19 severity. Asses the severity of the disease is an important thing to determine the management. Vitamin D is shown to have anti-inflammatory effect. Vitamin D can downregulate cytokines storm and also induce innate immune activity. Here we want to know about the correlation between level of vitamin D and disease severity of COVID-19.
Methods: Cross sectional study was observed 68 patient COVID-19 in Prof. Dr. I. G. N. G Ngoerah Denpasar hospital. They were asses with SCAP scoring system dan measured their vitamin D level at the same time. The correlation between two variable was analyze by Spearman correlation.
Results: Among those 68 Sample, the median age of the sample is 64 years old, and 52.9 % of them are male. There is correlation between level of vitamin D and severity of COVID-19, the coefficient correlation was -0.47 with p<0.001.
Conclusions: There is correlation between level of vitamin D and severity of COVID-19.

Keywords: COVID-19, Vitamin D, Inflammation

INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. The virus spread from Wuhan, Hubei province, China to all over the world in December 2019. On march 2020 WHO reported spread to 114 countries with 4291 death cases.[1] The pathological process that occurs in COVID-19 includes a wide spectrum of clinical manifestations, ranging from asymptomatic, mild symptoms (flu like symptoms), moderate symptoms and severe symptoms. Patients with COVID-19 often require treatment in an intensive room. The severity of COVID-19 symptom affected by the inflammation process and cytokine storm.[2]

Vitamin D well known function to help regulate serum calcium concentrations, also play importance role in inflammation process. Vitamin D enhances cellular innate immunity partly through the induction of antimicrobial peptides, including human cathelicidin, LL-37. Vitamin D also enhances cellular immunity by reducing the cytokine storm induced by the innate immune system. There for, we need to conduct study to know about the correlation between level of vitamin D serum and COVID-19 severity.[3]

METHODS

This study aims to find out correlation between level of vitamin D serum and COVID-19 severity. Cross sectional study was observed 68 COVID-19 patients in Prof. Dr. I. G. N. G Ngoerah Denpasar hospital in 2022. Sample chose with consecutive sampling from February 2022 until June 2022. The inclusion criteria were COVID-19 patients who confirm using RT-PCR, with age range 18 years old until 80 years old. COVID-19 patient who have been treated or

consume vitamin D was excluded. They were asses with SCAP scoring system for the COVID-19 severity and measured their vitamin D level at the same time. Sample distribution normality tested with Kolmogorov Smirnov; the result is not normally distributed. The correlation between two variables was analyze by Spearman correlation. Linier regression was conduct to know the effect of the confounding variables to the COVID-19 severity.

RESULTS

This study observed 68 COVID-19 patients in Prof. Dr. I. G. N. G Ngoerah Denpasar hospital. The median age of this study was 64 years old with IQR 22. From those 68 subjects we found that 52.9% are female and 47.1% are male. The median of vitamin D serum level is 16.25 ng/mL with IQR 9.5. SCAP score median of those sample is 17 with IQR 14. Three comorbid commonly found are hypertension (35 subject), diabetes (28 subjects), and cardiovascular disease (23 subjects). There are 33 subjects (48.5%) were vaccinated with COVID-19 vaccine, and the means onset of the disease is 6.59 days±2.13 SD. Here is the characteristic table of this study (Table 1 and 2).

The correlation between vitamin D serum level and two variable was analyze by Spearman correlation. There is negative significant correlation was found in this study, with the coefficient correlation-0.47. Here is the correlation chart of the two variables (Figure 1).
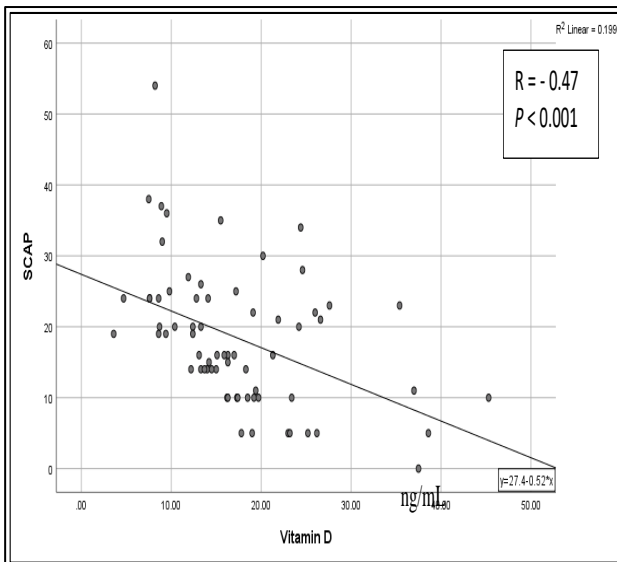

Figure 1: Correlation between vitamin D serum level and COVID 19 severity (SCAP score).

Multivariate analysis, Linier regression was conduct to know the effect of the confounding variables to the COVID-19 severity. We found that there is two confounding variable which significantly affect COVID-19 severity, those are onset of the disease and COVID-19 vaccination. Here is result of the multivariate analysis of this study (Table 3).

Table 1: Characteristic study.

Variables	Total, N (%)
Age (in year), median (IQR)	64 (22)
Sex	
Female	32 (47.1)
Male	36 (52.9)
Vitamin D serum level (ng/ml), median (IQR)	16.25 (9.50)
Vitamin D serum<20 ng/ml	49 (72.1)
Vitamin D serum ≥20 ng/ml	19 (27,9)
SCAP score, median (IQR)	17 (14)
SCAP score ≥10	60 (88.2)
SCAP score <10	8 (11.2)

IQR: Interquartile range; SCAP: Severe community acquired pneumonia.

Table 2: Comorbid COVID-19.

Comorbid	Total, N (%)
Hipertensi	35 (51.5)
Diabetes	28 (41.2)
Obese	11 (16.2)
HIV infection	2 (2.9)
Autoimune disease	1 (1.5)
Malignancy	2 (2.9)
Chronic kidney disease	22 (32.4)
Chronic liver disease	11 (16.2)
Cardiovascular disease	23 (33.8)
COVID-19 vaccination	33 (48.5)
Onset, mean±SD	6.59±2.13

Table 3: Multivariate analysis, confounding variable and COVID-19 severity (SCAP score).

Variables	β	P value	CI 95%	
			Lower bound	Upper bound
Vitamin D	0.63	<0,001	-1.0	-0.47
Hypertension	0.10	0.32	-2.0	6.19
Diabetes	-0.74	0.48	-5.5	2.6
Obese	0.036	0.74	-6.7	4.8
Malignancy	0.15	0.12	-2.5	2.0
Autoimmune disease	-0.56	0.59	-21.47	12.45
HIV Infection	0.07	0.47	-6.7	15.45
CLD	0.26	0.06	-0.341	11.0
CKD	-0.13	0.18	-7.08	1.42
Cardiovascular disease	-0.16	0.13	-7.81	1.06
Onset	0.23	0.029	0.11	2.02
COVID-19 vaccination	-0.36	0.001	-11.09	-2.90

β: Coefficient beta; CI: Confident interval.

DISCUSSION

Among 68 subjects the median age is 64 years old with IQR 22 years. RSUP Prof. Dr. I. G. N. G. Ngoerah

Denpasar was a referral hospital for those who diagnose with moderate COVID-19 until critically ill, it is also confirm by 88.2% among the subject have ≥10 SCAP score. Study by Statsenko, show that in the group population >65 years old, most of them have moderate to critically sign of COVID-19.[4]

Male subject is most common in this study, 36 subjects (52.9%), this can be related to male habit that can increase their exposure to SARS-CoV 2 virus, including smoking in public area, work outside home, and also drink alcohol with their friends.[5]

The median of vitamin D serum level is 16.25 ng/mL with IQR 9.5 ng/mL, 72.1% among them has vitamin D deficiency. Vitamin D insufficiency or deficiency is associated with higher risk of severe SARS-CoV-2 infection necessitating hospital admission.[6]

In this study we found that there is negative correlation between vitamin D serum level with COVID-19 severity (SCAP score), the coefficient correlation is -0.47 with p<0.001. Vitamin D was strongly related to inflammation process, whether it was innate immune nor adaptive immunity. Vitamin D improve differentiation, maturation and function of macrophage. Vitamin D deficiency reduce migration ability from neutrophil and reduce its antimicrobial effect. Vitamin D also play role in NK cell differentiation and its cytotoxicity. The role of vitamin D in adaptive immunity are directly affect proliferation, differentiation, and apoptosis lymphocyte B and T. Not only playing role in immunomodulator, vitamin D also playing role in direct antiviral effect. Vitamin D induce gen CAMP. Cathelicidin (LL-37) is an active form of CAMP. LL-37 bound with SARS-CoV-2 spike protein to prevent its binding with ACE2 receptor than prevent the virus entering host. LL-37 also can prevent viral replication.[3]

A meta-analysis study conducted by Danis et al discover that there is correlation between vitamin D and reduce COVID-19 severity.[7] Study in Galilee medical center Israel also found that there is correlation between vitamin D serum level and COVID-19 severity.[8]

Multivariate analysis in this study show that onset and vaccination significantly affect COVID-19 severity. COVID-19 symptoms can occur from day 2 until day 14 after exposure to SARS-CoV-2 virus. The symptom varied from common viral infection signs to severe sign such as ARDS. There are 3 phases of COVID-19, infection phase, pulmonary phase, and inflammation phase. In the last phase, or inflammation phase, there is involvement of other than the lung and also involvement of proinflammatory cytokines causing cytokine storm and severe symptom. The inflammation phase can occur onset day 7 until day 15, that is why onset of the disease is related to COVID-19 severity.[9]

COVID-19 vaccination is an effort to protect people from severe COVID-19 symptoms, hospitalization, and mortality. In this study, we found that vaccination affect COVID-19 severity. Vaccine injected to the body so that immune system can recognize pathogen by activating CD-4, T helper cell which can stimulate B cell to neutralize specific antibodies against viruses. A study observed any kind of COVID-19 vaccine show that all vaccines type effective to reduce COVID-19 severity.[10]

CONCLUSION

Vitamin D serum level have a significant negative correlation with COVID-19 severity (SCAP score).

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