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DOI: [10.31965/infokes.Vol21Iss2.1204](https://doi.org/10.31965/infokes.Vol21Iss2.1204)Journal homepage: <http://jurnal.poltekkeskupang.ac.id/index.php/infokes>**RESEARCH****Open Access****Difference of Cycle Threshold Value, Oxygen Saturation and D-dimer to COVID-19 Vaccination****Dhani Redhono Harioputro^{1a*}, Arsyi Dasa Ramadhan^{2b}, Evi Nurhayatun^{1c}, Satrio Budi Susilo^{3d}, Nurhasan Agung Prabowo^{4e}**¹ Division of Tropical Infection Disease, Department of Internal Medicine, Sebelas Maret University, Moewardi Hospital, Surakarta, Indonesia² Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia³ Department of Internal Medicine, Moewardi Hospital, Moewardi Hospital, Surakarta, Indonesia.⁴ Division of Rheumatology, Department of Internal Medicine, Sebelas Maret Hospital, Surakarta, Indonesia^a Email address: dhani_redhono@staff.uns.ac.id^b Email address: arsyidasa@gmail.com^c Email address: evi.nurhayatun@staff.uns.ac.id^d Email address: robertsatriyo@gmail.com^e Email address: dr.Nurhasan21@staff.uns.ac.id

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Abstract

Many factors can affect the prognosis of COVID-19 patients, and Cycle Threshold value can be used to estimate the amount of virus in the body. Oxygen saturation and D-dimer are important components in determining the severity. This study aims to analyze the difference of CT value, oxygen saturation, D-dimer, and degree of severity on vaccination state. This study is the observational analytic study of patients admitted to the isolation ward of a referral hospital in Surakarta, Indonesia. The analysis covered assessing the normality of the data, the Kruskal-Wallis correlation test, and ANOVA to assess the differences between variables. A total of 154 patients with, 65.6% of them did not participate in the full vaccination program. The results of the analysis showed a significant difference between the D-dimer and the degree of severity with a p-value of < 0.05 , while the CT value and oxygen saturation had no significant difference with the vaccination state. Vaccination showed a significant difference with D-dimer and the degree of severity of COVID-19 infection, so giving a complete vaccine can reduce the severity of COVID-19 patients, and we recommended to be able to complete the vaccine for the whole community.

Keywords: CT Value, Oxygen saturation, D-dimer, Degree of severity, COVID 19 Vaccination.***Corresponding Author:**

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1. INTRODUCTION

Corona Virus Disease 2019 (COVID-19) infection caused by Novel Beta Coronavirus (SARS-CoV-2), and having similar phylogenetic properties to SARS-CoV, is currently a global health problem (Hu et al., 2021; Matheson & Lehner, 2020; Yuen et al., 2020). The disease COVID-19, caused by infection with SARS-CoV-2, is associated with a series of physiopathological mechanisms that mobilize a wide variety of biomolecules, especially immunological ones (Costela-Ruiz et al., 2020; Li et al., 2020). The gold standard for infection diagnosis is real-time reverse transcriptase PCR (RT-PCR) (Kevadiya et al., 2021; Rao et al., 2020; Younes et al., 2020). Following the emergence of the COVID-19 pandemic, D-dimer was established as a possible predictor of prognosis for COVID-19 patients. Several studies have shown that D-dimer values at admission can predict disease severity (Soni et al., 2020; Tian et al., 2020; Zhang et al., 2020; Zhou et al., 2020). It has been reported that about 50% of patients have elevated D-dimer levels and abnormal D-dimer levels are associated with a poor prognosis (Guan et al., 2020; He et al., 2021; Wang et al., 2020).

Infectious illnesses, including COVID-19, are not immune to the wide-ranging impacts of climate change on health. By directly affecting the biological features of pathogens (e.g., growth, survival, and virulence) and their vectors, as well as indirectly favoring transmission through ecosystem modification and changes in human behavior, climatic conditions are becoming increasingly suitable for the transmission of multiple infectious diseases (Baker et al., 2022; Microbe, 2021). Infectious diseases ranging from vector-borne diseases (e.g., malaria, dengue fever, and leishmaniasis) to enteric infections and diarrhea (e.g., cholera, vibriosis, and rotavirus infection) to parasitic diseases like schistosomiasis and zoonotic disease like anthrax and also COVID-19 disease can all be exacerbated by rising temperatures and increased precipitation (Microbe, 2021; Redhono & Dirgahayu, 2016). SARS-CoV-2 growth and survival in the environment are more closely linked to environmental temperature and relative humidity. The combined temperature and humidity spectrum is critical for predicting COVID-19 outbreaks. COVID-19 infections are more common in areas with a greater population number (McEwen et al., 2022; Sasikumar et al., 2020).

Vaccination is one of the efforts to prevent COVID-19 infection. In Indonesia, vaccination coverage for dose one has reached 54.90%, which is 115.502.524 people and dose two has reached 33.18%, which is 70.113.618 people from the total population of Indonesia (Kementrian Kesehatan Indonesia, 2021). This study aims to analyze the relationship between vaccination history against D-dimer, CT value, oxygen saturation, and degree of infection.

2. RESEARCH METHOD

This study is a retrospective study on inpatients in the isolation room of RSUD dr. Moewardi Surakarta, Indonesia, during the second wave of the COVID-19 pandemic in July to September 2020 and was approved by the ethics committee of RSUD Dr. Moewardi no. 729/VII/HREC/2021. Vaccination history is known through history taking on each patient admitted. Research subjects were divided into three groups based on vaccination history. Vaccination history is divided into complete vaccination, namely people who have received two doses of vaccination, incomplete vaccination if they only received one dose of injection, and no vaccination if they have never received the first or second dose of vaccination.

The statistical analysis begins by assessing the normality of the data from four variables, namely D-dimer, CT value, saturation, and disease degree. Statistical analysis was carried out with a computer application using ANOVA correlation test on normally distributed data and Kruskal Wallis on abnormally distributed data to assess differences between variables.

3. RESULTS AND DISCUSSION

Data on COVID cases obtained was 154 cases with a mean age of 46.77 ± 14.74 where 65.6% (n=95) had never received a complete vaccination and vaccinated 34.3% (n=53). A non-parametric ANOVA test was performed to determine the difference between CT values and vaccination history. The mean in each group was complete vaccination 24.6 ± 6.6 ; incomplete vaccination 20.6 ± 3.7 ; and unvaccinated 25.2 ± 6.1 as shown in Table and Figure 1. The ANOVA test showed no significant difference (Asymp. Sig. = .24) in the three groups based on the vaccination history. The post hoc test also found no significant difference between groups. The Ct value represents the number of PCR cycles required to identify a SARS-CoV-2 positive patient. The presence of more copies of viral RNA in the sample is indicated by fewer cycles. As a result, we used the Ct value as a semiquantitative measure of viral load (Regev-Yochay et al., 2021). Our study showed no differences in CT values in the three observed groups.

Table 1. Analysis of the difference of the CT value with vaccination state

	Mean	SD	p-value ^a
Complete vaccine	24.6	6.6	= 0.24*
Vaccine once	20.6	3.7	
No Vaccine	25.2	6.1	

^aOne-way ANOVA, $\alpha = 5\%$

*Significance ($p < 0.05$)

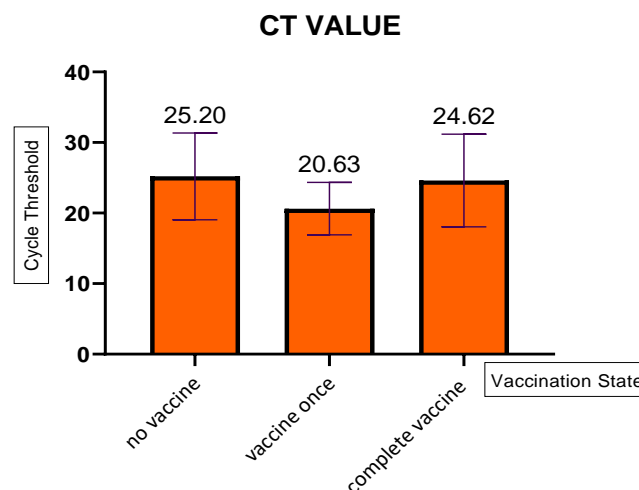


Figure 1. Mean of CT Value between each group.

The results of the analysis of age on the history of vaccination with nonparametric measurement Kruskal Wallis showed that there was a significant difference (Asymp. Sig. = .012) against the three groups based on the history of vaccination with a confidence interval of 95%, where p-value < 0.05 was considered significant.

The results of the D-dimer analysis of the history of vaccination with Kruskal Wallis' non-parametric measurement showed that there was a significant difference (Asymp. Sig. = .001) where the p-value < 0.05 was considered significant, with different mean in each group (complete vaccination = 1237.8 ± 2903 ; incomplete vaccination = 798.83 ± 514 ; and unvaccinated = 2637.6 ± 4220) as shown in Table 2 and Figure 2. D-dimer is one of the variables that is often used as a predictor of the severity of COVID-19. D-dimer is a specific degradation product produced in the hydrolysis of fibrin (Gorjipour et al., 2019). This may reflect the effect of coagulation during infection in infectious diseases. Several studies reported increased levels of D-dimer in patients with pneumonia, indicating a state of blood

hypercoagulability and indicating the presence of thrombosis (Arita et al., 2016; Tian et al., 2020).

Table 2. Analysis of the difference of D-dimer with vaccination state.

	Mean	SD	p-value ^a
Complete vaccine	1237.8	2903	= 0.001*
Vaccine once	798.83	514	
No Vaccine	2637.6	4220	

^aOne-way ANOVA, $\alpha = 5\%$
*Significance ($p < 0.05$)

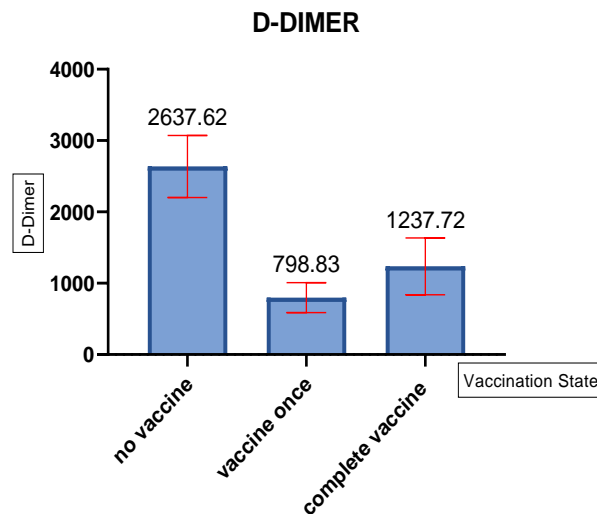


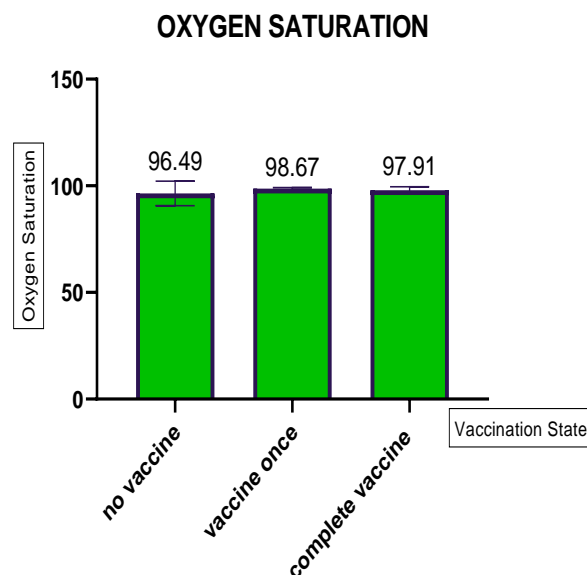
Figure 2. Mean of D-dimer value between each group.

D-dimer in critically ill patients with COVID-19 was significantly increased, with frequent clotting disorders and microthrombotic formation in peripheral blood vessels (Jin et al., 2020). The increase in D-dimer in the literature on viremia and cytokine storm is due to an increase in pro-inflammatory cytokines (IL-2, IL-6, IL-8, IL-17, TNF- α) that cannot be controlled by anti-inflammatory factors that will cause inflammation, leads to overactivation of the coagulation cascade (Wool & Miller, 2021). A recent study found that the development of laboratory results, particularly D-dimer, in hospitalized patients accurately predicts mortality and severity of COVID-19 (Qeadan et al., 2021). We also analyzed the relationship between vaccination history and D-dimer level and obtained a p-value of .001 which can be concluded that vaccination history is closely related to the D-dimer level in COVID-19 patients.

The results of the saturation analysis of the history of vaccination obtained a p-value of 0.202, which means that there was no significant difference between the history of vaccination and the saturation at admission. The mean saturation between each group are complete vaccination = 97.91 ± 1.7 ; incomplete vaccination = 98.7 ± 0.52 ; and unvaccinated = 96.44 ± 5.7 as shown in Table 3 and Figure 3. COVID-19 has various clinical manifestations, with 80% of cases being mild, 15% having lower respiratory tract diseases such as pneumonia, and less than 5% having severe symptoms (Deming & Chen, 2020). In patients with severe symptoms, there is often damage to the respiratory system, which causes oxygen saturation to decrease, this is then used as a component in assessing the severity of COVID-19. Parameters of the progression of this infection can also be assessed by examination of D-dimer.

Table 3. Analysis of the difference of oxygen saturation with vaccination State

	Mean	SD	p-value ^a
Complete vaccine	97.91	1.7	= 0.202*
Vaccine once	98.7	0.52	
No Vaccine	96.44	5.7	

^aOne-way ANOVA, $\alpha = 5\%$ *Significance ($p < 0.05$)**Figure 3.** Mean of oxygen saturation between each group.

COVID-19 vaccination is an important effort in controlling the pandemic. It is hoped that by carrying out complete vaccinations, the transmission rate of COVID-19 can be controlled, but there are still some cases with complete vaccinations, still infected with COVID-19 and must be hospitalized in a hospital isolation room. In several studies, vaccination has been shown to reduce the risk of hospitalization. Understanding the relation on the effectiveness of vaccines in protecting individuals needs to be further deepened. Vaccination was not one hundred percent able to protect individuals against COVID-19, given the many discoveries and developments of new virus variants, especially Variant of Concern B.1.1.7 (alpha variant) (Graham et al., 2021).

The results of our study analysis found that vaccination can reduce the severity of COVID-19 disease ($p = 0.001$) with a 95% confidence interval. The mean in each group was complete vaccination 1.25 ± 0.48 ; incomplete vaccination 1.67 ± 0.52 ; and unvaccinated 1.81 ± 0.72 as shown in Table 4 and Figure 4.

Table 4 Analysis of the difference of degree of severity with vaccination state

	Mean	SD	p-value ^a
Complete vaccine	1.25	0.48	= 0.001*
Vaccine once	1.67	0.52	
No Vaccine	1.81	0.72	

^aOne-way ANOVA, $\alpha = 5\%$ *Significance ($p < 0.05$)

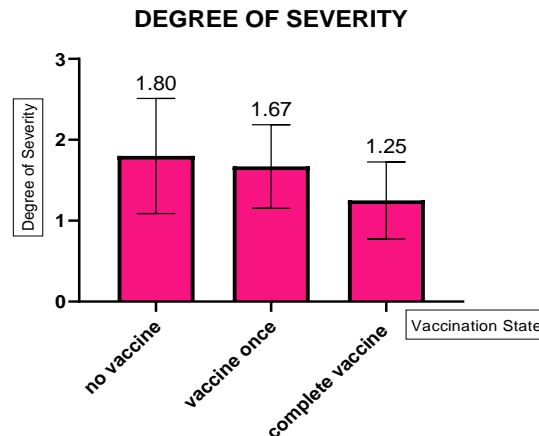


Figure 4. The mean of Degree of Severity between each group.

However, due to the emergence of climate change, a virus could also spread faster and the chance of mutation could be concerning. Several new variants of interest have been shown to increase in reducing the neutralizing effect of the vaccine taken from in vitro samples (Kustin et al., 2021) and lead to increased infection rates in vaccinated individuals compared to the first variant in the initial findings from a case-control study (McEwen et al., 2022).

The weakness of this study is the nature of the study, which is a retrospective study, so that selection bias is the main weakness of our study. Only hospitalized individuals were included in the study, excluding asymptomatic patients with high oxygen saturation who were not hospitalized according to hospital regulations. Incomplete laboratory testing and medical records so that some cases were declared eligible for rejection. The duration between the onset of the disease course and admission to the hospital can impact the outcome of the variables studied. This study was also only carried out at one hospital center so that it could reduce the ability to provide an overview in general.

4. CONCLUSION

Vaccination showed a significant difference with D-dimer and the degree of severity COVID-19 cases, so giving a complete vaccine can reduce the severity of COVID-19 patients and we recommended to be able to complete the vaccine for the whole community.

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