(RESEARCH ARTICLE)

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Chest imaging of COVID-19 patients amongst diverse vaccination status: A comparative study using Brixia Score

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Abstract

Background: Covid-19 vaccination has reached more than 132 million people in Indonesia since its first outbreak in March 2020. However; its effects on immunity are still lack of evidence. Covid-19 cases reached a significant increase in June 2021 and decreased in November 2021. In early 2022; it again recorded an increase. Seeing this phenomenon; this study investigates the differences of Covid-19 Patients' severity levels over their vaccination status.

Objective: This study examines the differences of severity level of chest x-ray imaging in covid-19 patients treated at Dr. Moewardi Hospital in three periods of time.

Methods: A total of 89 covid-19 cases were collected from 3 different vaccination status: (1) 30 non-vaccinated patients (group A); (2) 30 patients treated for covid-19 after 1-3 months post-vaccination (group B); (3) 29 treated for covid-19 after more than 6 months post-vaccination (group C). Patients with type-II diabetes mellitus; heart failure or autoimmune disease were excluded. Severity level is based on chest x-ray examination by calculating the Brixia score by 3 examiners. All assessment results were analysed using the Kruskall-Wallis test followed by the Mann-Whitney post-hoc test.

Results: A total of 8 male (26.7%) and 22 female (73.3%) patients in group B had lower Brixia scores with mean score 2.94 ± 0.25 compared to 29 patients (55% male and 45% female) in group C with mean score 4.90 ± 0.27 with a significant difference ($p = 0.001$). The Brixia score with the highest average was found in group A (non-vaccinated) with mean value 5.77 ± 0.31 showing a significant difference from groups B and C ($p<0.05$).

Conclusion: Vaccine administration status showed different Brixia scores; whereas longer duration from vaccination showed higher score. Unvaccinated patients recorded the most severe condition. Booster vaccination is strongly recommended to obtain the best immunity level.

Keywords: Covid-19; Brixia Score; Vaccination; Patients

1. Introduction

Corona virus disease-19 (covid-19) first appeared in Wuhan, China at the end of December 2019 with symptoms of fever, cough, and muscle aches (1). This disease manifests in a variety of conditions ranging from mild to severe symptoms. The covid-19 death rate varies between countries, while the number of infected humans cannot be

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ascertained considering that a number of cases are asymptomatic infections (2). Radiological examination has an important role in the diagnosis of covid-19. Imaging techniques such as chest x-ray (CXR), computed tomography (CT) scan, ultrasound (US), and magnetic resonance imaging (MRI) have been used to diagnose covid-19. In everyday life, the CXR examination is considered more practical, especially if it is combined with a certain assessment system (3) such as the Brixia assessment. The Brixia scoring system has been widely used as a tool to monitor the severity and progression of covid-19. The Brixia scoring system assesses pulmonary disorders due to covid-19 on a severity scale totalling 18 points.

Covid-19 vaccination is expected to be a solution to raise individual and herd immunity against covid-19 virus. It prevents the vaccinated patients experiencing severe symptoms and reducing morbidity (4). In Indonesia, vaccine coverage has reached 132 million people in early March 2022. In fact, someone who has received the vaccine still has the potential to be infected by covid-19 (5). Unexpectedly, the third wave happened in early 2022, with an incidence rate of 32,211 new cases per day. Consequently, the vaccine effectiveness was questioned. In addition, the waning immune response has been proven after 28 weeks prior to vaccination (6). This study investigates the differences of covid-19 patients' severity levels over their vaccination status.

2. Methods

The research subjects were 89 covid-19 patients hospitalized at the Dr. Moewardi general hospital Indonesia evidenced by PCR examination. This research was conducted through ethical approval from the Ethics Commission of Dr. Moewardi general hospital which refers to the principles of the Declaration of Helsinki. Purposive sampling was applied by taking covid-19 patients aged 18 to 65 years who did not have comorbid diseases such as diabetes mellitus, heart failure, or autoimmune diseases and had chest x-ray data which was carried out within 24 hours of the patient administered to the hospital. Patients' data were taken from December 2020 to February 2022. The samples were divided into group A (non-vaccinated), group B (treated for covid-19 after 1-3 months post-vaccination), and group C (treated for covid-19 after more than 6 months post-vaccination). The assessment of the Brixia score on the chest x-ray was carried out by 3 examiners by observing the results of the chest x-ray through the Picture Archiving Communication System (PACS). The three examiners had at least one year of experience in reading chest X-rays under the supervision of a thoracic radiologist with more than 10 years of experience. The assessment was carried out blindly so that the examiners did not know the origin of the group from which the CXR was assessed. Then, the Brixia scores from all the examiners were calculated and compared using the Kriskall-Wallis test with the p value being considered to be significantly different if the value was less than 0.05.

3. Results

The results of the study involved 89 covid-19 patients who were hospitalized at Dr. Moewardi general hospital, consisted of 42 male patients (47%) and 47 female patients (53%). A total of 35 subjects (39%) were aged between18-35 years old, 16 subjects (18%) were aged between 35-40 years old, and the remaining 38 subjects (43%) were aged between 40-65 years old. The data of sex and gender of subjects are presented in table 1. While, the results of the Brixia score assessment in each group are presented in Table 2.

Table 1 Data of sex and age of subjects

	Criteria	Total	Percentage
1.	**Sex**		
	Male	42	47
	Female	47	53
2.	**Age**		
	18-35 years	35	39
	35-40 years	16	18
	40-65 years	38	43

Table 2 The result of Brixia score measurement of all groups

	Group	Highest score	Lowest score	Mean ± SD
1.	A	12,00	2,00	5,78 ± 0,31
2.	B	13.00	0.00	2.94 ± 0.25
3.	C	14.00	0.00	4,94 ± 0,27
				p = 0.001

The normality test was first carried out to see the normality of the data distribution with the results of the data being not normally distributed. Furthermore, the Kruskall-Wallis non-parametric test was carried out with a p value of <0.05 which means that between each group there is a significant difference related to the results of the Brixia score. Based on the mean value, the lowest score was in group B, followed by group C. Meanwhile, group A had a higher Brixia score than groups B and C.

4. Discussion

The first covid-19 in Indonesia was reported in two cases on March 2, 2020. The mortality rate for covid-19 in Indonesia was 8.9% and it was the highest in Southeast Asia. The total number of positive covid-19 cases in Indonesia as of September 23, 2021 (the second wave) was 4,201,559 cases, with a total of 141,114 deaths or 3.4% of the total cases (7). SARS Cov-2 is an RNA virus with a particle size of 120-160 nm (8). Covid-19 infection can be divided into three clinical stages of the disease. Stage I is the asymptomatic state (early phase 1-2 days of infection). The inhaled SARS-CoV-2 virus probably binds to epithelial cells in the nasal cavity and begins to replicate. RT-PCR values for viral RNA may be useful for predicting viral load and subsequent infectivity and clinical course. Furthermore, in stage II, the virus spreads and migrates to the respiratory tract along the airway, and a stronger adaptive immune response is generated. Stage III has hypoxia, infiltrates, ground glass opacity, and progression to ARDS in approximately 20% of infected patients. Under these conditions, the virus has reached gas exchange units in the lungs and infects type II alveolar cells. The infected alveolar units tend to be located peripherally and sub-pleural. SARS-CoV spreads inside type II cells, large numbers of viral particles are released, cells undergo apoptosis and die (9). Histopathological results from SARS and covid-19 were diffuse alveolar damage with fibrin-rich hyaline membranes and multiple multinucleated giant cells. Suboptimal wound healing causes more severe scarring and fibrosis than other forms of ARDS (10). This pathogenesis is the basis for determining Brixia's scoring in covid-19 cases.

The Brixia score is a chest x-ray (CXR) scoring system specifically designed for the semi-quantitative assessment of covid-19 using a 0-18 severity scale according to the extent and characteristics of the lung abnormalities that appear in the patient (11). The Brixia score index is specially designed for hospitalized patients with covid-19 infection confirmed by real-time PCR. Other CXR findings such as pleural effusion and hilar enlargement that were not included in the scoring system, were recorded in the descriptive section of the CXR report.

Post-vaccination antibody titres decreased along with the time. The phenomenon of waning immunity in cases of Sars-Cov2 infection showed that after 28 weeks prior to vaccination, antibody levels decreased, although it cannot be concluded whether protection against the virus also decreased equivalently (6). This phenomenon is not only found in cases of covid-19 but also applies to several other infectious diseases for which vaccines have been found. To increase the level of specific antibodies against the virus, a booster vaccination is needed. In this case, reinfection in patients can also be a trigger for the production of more antibodies, although of course, this is quite worrying considering that the virulence level is not always as strong as the body's immunity at that time, so it is feared that moderate or even severe conditions will occur. Booster vaccination showed an increase in the humoral immune response in the adaptive immune system.[11] Therefore, booster vaccines have become a government program in various countries. This study also supports the statement above by looking at the condition of the covid-19 patients being treated at the hospital and their vaccination status.

Vaccination triggers the production of specific antibodies against covid-19 so as to provide optimal protection against SARS-CoV-2 infection. Booster vaccinations are given to increase antibody levels in the adaptive immune system so that the body continues to provide optimal protection even though second vaccination is not as effective as first vaccination (with the same regiment) in improving immune responses of covid-19 patients (12). However, a smaller increase in

antibody titre does not necessarily decrease protection against viral infection. Wanning immunity that occurs naturally still requires a booster to maintain optimal protection, especially in conditions where infection occurs widely.

Many countries have experienced three wave patterns in cases of the covid-19 disease. Differences in age range and disease severity have been reported, although the comparative characteristics of the three waves remain largely unknown. The existence of several waves of covid-19 cases provides insight into vaccinations that have begun to be widely given to the public before the second wave. The weakness of this research is that the number of research samples is still limited. This study is a unicentric study conducted in one hospital and covers only a small geographic area. Therefore, it is still necessary to do further research on a larger scale so that the data obtained is more representative. Research with larger subjects and scales is needed so that it is easier to analyse the data and reduce the risk of bias in the results.

5. Conclusion

We can assess the evidence of the pulmonary manifestation through chest x-ray imaging with severity level assessment using the Brixia scoring system. Vaccine administration status showed lower Brixia score, whereas longer duration from vaccination showed higher score. Covid-19 patients received two doses of the vaccine have better resistance to the covid-19 virus than unvaccinated patients. Unvaccinated patients recorded the most severe condition. Therefore, booster vaccination is strongly recommended to obtain the best immunity level.

Compliance with ethical standards

Disclosure of conflict of interest

By this statement, all authors who consist of Muchtar Hanafi, Ida Prista Maryetty and Widiastuti Soewondo have no conflict of interest regarding this manuscript publication.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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