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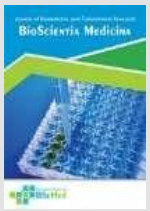

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Correlation of the Adverse Event Following Immunization with the Severity of COVID-19 Infection in Health Care Workers in Padang

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A B S T R A C T

Background: Effective countermeasures to control the current COVID-19 pandemic are the implementation of health protocols and vaccinations. The problem that must be a concern after vaccination is post-immunization co-occurrence (AEFI), including COVID-19 vaccination. Another issue that is also a concern after vaccination is the incidence of being infected with COVID-19. The purpose of this study was to determine the incidence of post-vaccination COVID-19 infection in health workers in the city of Padang and its association with the incidence of COVID-19 vaccine AEFIs. **Methods:** The study used a descriptive-analytic design with a retrospective cohort method. The research will be carried out in all hospitals in Padang, and sampling will be carried out for 2 months, from November to December 2021. Officers who are confirmed to have COVID-19 after vaccination and meet the inclusion criteria are healthcare workers who have received at least 2 vaccines and are willing to fill out a Google form. **Results:** The characteristics of health workers in Padang who were confirmed to have COVID-19 after 2 vaccinations were mostly (68.1%) early adults (26-35 years), the sex was mostly female as much as 77.3%, and most professions were workers. Paramedics (nurses or midwives) as much as 57.0%. The most comorbid obesity is as much as 3.4%. Nutritional status assessed by BMI showed that obesity (37.7%) and normal nutritional status (32.9%) had almost the same proportion. Almost all health workers with or without AEFI experience mild COVID-19, as many as 98%, and experience COVID-19 infection 28 days after vaccination. **Conclusion:** The incidence of AEFI is not related to the severity of post-vaccination COVID-19 infection in health workers in Padang.

1. Introduction

Coronavirus Disease 2019(COVID-19) is an infectious disease caused by severe Acute Respiratory Syndrome Coronavirus 2(SARS-COV-2), a new type of coronavirus that has never been previously identified in humans. The World Health Organization (WHO), on August 5th, 2021, the cumulative number of COVID-19 cases globally surpassed 200 million. The largest proportionate increases in new cases were reported by the Americas Region at 14%, and the Western Pacific Region at 19%, with 1.3 million and over 375,000 new cases respectively reported.1 In Indonesia, from January 3rd, 2020, to August 13th, 2021, there were 3,804,943 confirmed cases of COVID-19, with 115,096 deaths (3.02%) reported to WHO. COVID-19 cases in West Sumatera until August 15th, 2021, recorded 81,325 cases and 1,794 (2.2%) deaths.[3] Data on COVID-19 monitoring in Padang on August 15th, 2021, the number of confirmed cases of positive COVID-19 was 39,011, of which 35,140 cases recovered (90.1%), and 499 cases died (1.2%). Currently, there are 3327 confirmed cases of COVID-19 in Padang, of which 2207 are symptomatic and 1165 are asymptomatic.[1-4]

Effective countermeasures to control the current COVID-19 pandemic are in the form of implementing health protocols and vaccinations. SARS-CoV-2 vaccination is the hope of providing herd immunity. Based on the recommendation of the Indonesian Technical Advisory Group on Immunization (ITAGI), group immunity can be achieved if vaccination coverage reaches 70% of the population. Vaccination is carried out in stages, initially prioritizing health workers, public officials and the elderly, vulnerable communities, and other community groups. Vaccination in Indonesia itself started on January 13th, 2021, and is expected to be completed in March 2022. Until August 9th, 2021, 77,541,967 doses have been vaccinated.[2] Health workers (nakes) who have undergone vaccination are 1,468,764 people (97%) of the total health workers in Indonesia, namely 1,500,541 people. This number has exceeded the COVID-19 immunization target set by the government as much as 1.46 million.[5] The problem that must be a concern after vaccination is post-immunization co-occurrence (AEFI), including COVID-19 vaccination. The National AEFI Commission recorded 229 serious AEFIs due to COVID-19 vaccination as of May 16th, 2021. Of the 229 serious AEFIs, 221 (96%) were related to the use of the Sinovac vaccine, and 18 (4%) were related to the AstraZeneca vaccine. Meanwhile, there were 10,627 reports of non-serious AEFI reports. A total of 9,378 (88%) related to the use of the Sinovac vaccine, and 889 (12%) related to the use of the AstraZeneca vaccine. Reported non-serious AEFIs include dizziness, nausea, muscle pain (myalgia), joint pain (arthralgia), pain at the injection site, malaise, and fever.[6] Another issue that is also a concern after vaccination is the incidence of being infected with COVID-19. Based on Cristina Menni's research, data obtained, 3106 (2.99%) of 103,622 individuals who were vaccinated and 50,340 (10.8%) of 464,356 controls who were not vaccinated tested positive for SARS-CoV-2. A significant reduction in the risk of infection was seen starting 12 days after the first dose, reaching 60% (95% CI 49–68) for Oxford- AstraZeneca and 69% (66–72) for Pfizer-BioNTech at 21–44 days and 72% (63–79) for Pfizer-BioNTech after 45– 59 days.[7-10] There is no known exact data regarding the incidence of post-vaccination COVID-19 infection in Padang. Therefore researchers are interested in knowing the incidence of post-vaccination COVID-19 infection in health workers in the city of Padang and associated with the incidence of COVID-19 vaccine AEFIs.

2. Methods

The study used a descriptive-analytic design with a retrospective cohort method. The research will be carried out in all hospitals in the city of Padang, namely: Dr. M. Djamil General Hospital, Padang City Hospital, Unand Hospital, SPH, BMC Hospital, Hermina Hospital, Yos Sudarso Hospital, Ibnu Sina Hospital, Army Hospital, Bhayangkara Hospital, Naili Hospital DBS, Selaguri Hospital, Aisyiyah Hospital with sampling carried out for 2 months, from November to December 2021. Officers who are confirmed to have COVID-19 after vaccination and meet the inclusion criteria are officers who have received at least 2 vaccines and are willing to fill out a Google form. Data is collected and processed by a computerized system. Categorical data is displayed in the form of a frequency distribution. To assess the relationship, the Chi-square test was used to determine the significance, followed by multiple logistic regression with univariate analysis. Kaplan-Meier analysis was used to determine the time of occurrence of post-vaccination COVID-19 infection.

3. Results

The data used for this study were obtained from the G-form, which was filled out by 1003 health workers who served in public hospitals in the city of Padang. There were 941 health workers who received the vaccine twice. A total of 25 questionnaires were issued because they were filled out by the same health worker, so the remaining 916 of this number, 213 health workers (23.2%) were confirmed to have COVID-19 after vaccination. Six health workers were excluded due to incomplete G-form filling (1 health

worker did not include height data, 3 health workers mentioned weight (body weight) data that was not appropriate for adult age, and 2 health workers did not mention the type of comorbid), so the total sample of the study was 207. Characteristics of health workers in Padang (Table 1) who confirmed COVID-19 after 2 vaccinations were mostly (68.1%) early adults (26-35 years) and only 0.5% of health workers in the late elderly group (56-65 years). Most of the sexes are women, as much as 77.3%, and the most professions are paramedics (nurses or midwives), as much as 57.0%, while administrative staff and students are 3.9% each. Health workers who have confirmed post-vaccine COVID-19 and have comorbidities are 12.6%, with the most comorbid obesity, which is 3.4%. Nutritional status assessed by BMI showed that obesity (37.7%) and normal nutritional status (32.9%) had almost the same proportion, while underweight health workers had the least proportion, namely 6.8%. The incidence of AEFI in health workers who were confirmed to have COVID-19 after the vaccine in Padang was 23.7%.

Table 1. Distribution of the characteristics of health workers in Padang confirmed by COVID-19 post-vaccination.

Characteristics	n	n(%)
Age		
17-25 years old	26	12.6
26-35 years old	141	68.1
36-45 years old	32	15.5
46-55 years old	7	3.4
56-65 years old	1	0.5
Gender		
Woman	160	77.3
Labor type		
Medical	54	26.1
Paramedic	118	57.0
Support staff	19	9.2
Administration staff	8	3.9
Student	8	3.9
Comorbid		
Yes	26	12.6
Comorbid type		
Hypertension	6	2.9
Diabetes mellitus	2	1.0
Cerebrovascular	1	0.5
Cardiovascular	6	2.9
Liver disease	1	0.5
Kidney illness	1	0.5
Pulmonary TB	0	0.0
Asthma/COPD	6	2.9
Immunodeficiency	1	0.5
Obesity	7	3.4
Malignancy	1	0.5
Nutritional status		
Underweight	14	6.8
Normal	68	32.9
Overweight	47	22.7
Obesity	78	37.7
AEFI incident		
AEFI	49	23.7
The severity of COVID-19 infection		
Mild	200	96.6
Moderate	7	3.4
Critical	0	0.0
Time of occurrence of being infected with COVID-19		
14 days	24	11.6
15-27 days	13	6.3
> 27 days	170	82.1

Table 2. Analysis of the relationship between AEFI Incidence and the severity of COVID-19 infection post-vaccination among healthcare workers in Padang.

AEFI incident	Severity of COVID-19 Infection, n			p-value*
	Mild	Moderate	Critical	
AEFI	48	1	0	1.000
No AEFI	152	6	0	

*Fisher exact test.

The relationship between the incidence of AEFI in health workers who have confirmed COVID-19 after vaccination with the severity of COVID-19 infection is presented in Table 2. Almost all health workers with or without AEFI experienced mild COVID-19, namely 48 and 152, and there were no health workers with severe COVID-19. Fisher's exact test results obtained p value = 1,000 which indicates that the incidence of AEFI is not related to the severity of post-vaccination COVID-19 infection among health workers in Padang.

4. Discussion

The characteristics of health workers in Padang who were confirmed to have COVID-19 after 2 vaccinations were mostly (68.1%) early adults (26-35 years) and only 0.5% of health workers in the late elderly group (56-65 years). This is in accordance with the research of Hall et al. in the United Kingdom, which states that most AEFIs occur at the age of 46 years. The definition of the working age in Indonesia is the population aged 15- 64 years, so in this study, many characteristics were found in health workers aged 26 to 65 years. The age for the workforce is between 20 to 40 years. This age is considered very productive for the workforce because if the age is below 20 years, the average individual still does not have sufficient skill maturity and is still in the educational process. In this study, there were few health workers in the late elderly group. This is because the retirement age set by the government is 56 years. The highest gender is female, as much as 77.3%. This is in accordance with other research that the highest incidence of AEFI in health workers occurs in women (65%). Similar results were also obtained in a study by Menni et al. that the incidence of confirmed COVID-19 post-vaccination was found to be the most in women, namely 69.6%.[11,12]

Redailli et al. found that, in general, there were differences between the immune responses of women and men. Women can induce a stronger immune response than men. In addition, in women, the antibody titer in the vaccine was found to be twice as high as in men. Differences in the immune system between men and women are caused by hormonal factors and the X chromosome. Female hormones (estrogens) can form the immune system. This is because women are biologically structured to give birth to children and must protect the unborn baby. The X chromosome contains genes related to immunity. Men have one X chromosome and one Y chromosome, and women have two X chromosomes, therefore twice as many immune-related genes. This characteristic causes women to have a greater capacity to produce antibodies. In this study, the highest incidence of AEFI among health workers infected with COVID-19 was in women. This was because the number of research samples was mostly female. Most professions are paramedics (nurses or midwives), as much as 57.0%. This is because, based on the Indonesian Health Profile in 2020, it was found that the distribution of hospital health workers in Indonesia was found to be mostly nurses at 50.79%, followed by midwives. The risk of exposure to COVID-19 in health workers occurs due to exposure to infected patients, excessive workload, poor infection control, and pre-existing medical conditions (comorbid). Transmission of disease to health workers is related to the number of patients with inadequate room availability, lack of facilities in isolation rooms, and environmental contamination.[11-13]

The risk of exposure to health workers from COVID-19 is divided into 4 levels, namely low, medium, high, and very high. Low rates in jobs that do not require contact with suspected or confirmed COVID-19 patients or people who have minimal occupational contact with the public. Moderate level of frequent work and/or close contact with infected cases or suspected COVID-19 patients or people in contact with the general public. High levels of delivery health workers and support staff who are exposed to COVID-19 patients, patient transport workers, or corpse workers who are exposed to patients or the bodies of COVID-19 patients. Very high levels in health workers exposed to aerosols or health workers in laboratory personnel who collect or handle specimens. Health workers who have confirmed post-vaccine COVID-19 and have comorbidities are 12.6%, with the most comorbid obesity, which is 3.4%. Nutritional status assessed by BMI showed that obesity (37.7%) and normal nutritional status (32.9%) had almost the same proportion, while underweight health workers had the least proportion, namely 6.8%. Research by Menni et al. stated that the risk of infection was lower in people with normal BMI and underweight compared to obese people.[14]

Obesity is one of the comorbidities that can increase the morbidity and mortality of COVID-19 in a person. Obesity can cause disruption of the secretion process of the human immune system, such as cytokines, interferons, and adipokines, all of which are pro-inflammatory systems that can increase the inflammatory response in the body. Dysregulation of leukocytes and macrophages in the body causes disruption of the body's response to the entry of antigens. Obesity itself is known to induce an increase in IL6 and TNFα, so macrophage infiltration into adipose tissue is excessive. Obesity causes a disturbance in the body's immune response, thereby reducing the production of cytotoxic cells in immunocompetent cells, which are the main cells as antivirals. The increase in adipose cells in obese patients is caused by more ACE-2 receptors than in the lungs, so the risk of a person's severity of experiencing COVID-19 infection is higher. The incidence of AEFI in health workers who were confirmed to have COVID-19 after the vaccine in Padang was 23.7%. Research by Basuki et al. at the Yogyakarta Hospital was conducted on 572 people who received Sinovac vaccine immunization, and there were 54.5% reported experiencing AEFI, and 45.5% reported not experiencing any AEFI symptoms. Almost all health workers with or without AEFI experienced mild COVID-19, namely 98% and 96.2%, and there were no health workers with severe COVID-19. Fisher's exact test results obtained p value = 1,000 which indicates that the incidence of AEFI is not related to the severity of post-vaccination COVID-19 infection among health workers in Padang. Research by Pawar et al. found the same thing the mildest clinically confirmed COVID-19 degrees were mild (69.23%). The severity of COVID-19 can be affected by an infection acquired before vaccination or before antibodies are formed, recent mutations and variants, age of antibodies after vaccination, immunosuppression, and steroid use. Mutations of newer viral strains increase transmission and the ability to evade antibody systems. The mutation that occurs is the N439K mutation which is located in the receptor binding motifs (RBM). The SARS-CoV-2 virus spike protein, which is immunodominant and is the main target of virus-neutralizing antibodies that are formed either by viral infection or by injection with vaccines. Mutations can increase the affinity of the virus for the ACE-2 receptor in humans. Confirmed time for COVID-19 in health workers after vaccination is 28 days after vaccination. Another study by Keehner et al. observed SARS-CoV-2 infection after vaccination in healthcare workers in California. From December 16th, 2020, to February 9th, 2021, 36,659 health workers received the first dose of the vaccine, and 28,184 of them (77%) received the second dose. 379 vaccinated health workers tested positive for SARS-CoV-2 at least 1 day after vaccination, and the majority (71%) of these people tested positive within the first 2 weeks after the first dose. Khoury et al. found that one month after the second dose of the

vaccine, antibody titers decreased slowly thereafter. It was proved that four months after the second dose, the median titer level was 6% of the maximum median value.[15-18]

5. Conclusion

Health workers in Padang who are confirmed COVID-19 after two vaccinations are mostly women aged 26-35 years, and some are paramedics who have no comorbidities and obese nutritional status. The degree of severity of COVID-19 infection after two vaccinations is mostly mild. There was no significant relationship between the incidence of AEFI and the severity of COVID-19 infection. Most health workers experienced COVID-19 infection after 28 days post-vaccination.

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